EPA Jacket 11556-150

Vol.2

Material to be added to an e-Jacket/Jacket

Reg. No. 11556-150

Description: _____

_____

1. ☐ Placement within the e-Jacket/jacket:
   - ☐ Default: (chronological, top = newest)
   - ☐ File Location: (PDF page number, i.e., "before page 45")

   _____

   _____

2. ☐ Send to Data Extraction contractors this material:
   - ☐ Newly stamped accepted label
   - ☒ Notification
   - ☐ New CSF
   - ☐ Other: _____

3. Attach this coversheet to the top of the material or jacket. It must be well organized and clipped together, NOT STAPLED. Then give the material with this coversheet to staff in the Information Services Center (Room S-4900).

Reviewer's Name: Sam Daniel

Phone: 703 305-5409 Division: RD

Date: 8/19/2013

Created August 19, 2008

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

JUL 19 2013

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

Mr. J. Todd Frank
Bayer Health Care LLC
Animal Health Division
P.O. Box 390
Shawnee Mission, KS 66201

Subject: Addition of Alternate Brand Names

Dear Mr. Frank:

The Agency is in receipt of your Application(s) for Pesticide Notification under Pesticide Registration Notice (PRN) 98-10 dated August 9, 2013 for:

EPA Registration 11556-150

Advantage II Kitten (Alternate Names: ExpertCare Flea Protection Kitten
ExpertCare Topical Flea Protection Kitten
ExpertCare Kitten Flea Protection
ExpertCare Kitten Topical Flea Protection)

The Registration Division (RD) has conducted a review of this request of applicability under PRN 98-10 and finds that the label changes(s) requested falls within the scope of PRN 98-10. The label has been date-stamped "Notification" and will be placed in our records.

If you have any questions, call me at 703 305-5409 or electronically at daniel.dani@epa.gov.

Sincerely,

Dani Daniel
Registration Division (7504P)
Insecticide/Rodenticide Branch

NOTIFICATION

Please read instructions on reverse before completing form. Form Approved. OMB No. 2070-0060

EPA United States Environmental Protection Agency Washington, DC 20460

JUL 19 2013

☐ Registration ☒ Amendment ☐ Other:

OPP Identifier Number

Application for Pesticide - Section I

1. Company/Product Number	2. EPA Product Manager	3. Proposed Classification
11556-150	Venus Eagle	☒ None ☐ Restricted
4. Company/Product (Name)	PM#	
Advantage II Kitten	01	

5. Name and Address of Applicant *(Include ZIP Code)*
Bayer HealthCare LLC, Animal Health Division
PO Box 390
Shawnee Mission, KS 66201

☐ *Check if this is a new address*

6. **Expedited Review.** In accordance with FIFRA Section 3(c)(3)(b)(I), my product is similar or identical in composition and labeling to:
EPA Reg. No. _____
Product Name _____

Section - II

☐ Amendment – Explain below.
☐ Resubmission in response to Agency letter dated _____
☒ Notification - Explain below.
☐ Final printed labels in response to Agency letter dated _____
☐ "Me Too" Application
☐ Other - Explain below

Explanation:
Notification per PR Notice 98-10: Addition of alternate brand name.

This notification is consistent with the provisions of PR Notice 98-10 and EPA regulations at 40 CFR 152.46, and no other changes have been made to the labeling or the confidential statement of formula of this product. I understand that it is a violation of 18 U.S.C. Sec. 1001 to willfully make any false statement to EPA. I further understand that if this notification is not consistent with the terms of PR Notice 98-10 and 40 CFR 152.46, this product may be in violation of FIFRA and I may be subject to enforcement action and penalties under sections 12 and 14 of FIFRA.

Section - III

1. Material This Product Will Be Packaged In:

Child-Resistant Packaging	Unit Packaging	Water Soluble Packaging	2. Type of Container
☐ Yes* ☐ No	☐ Yes ☐ No	☐ Yes ☐ No	☐ Metal ☐ Plastic ☐ Glass ☐ Paper ☐ Other (Specifiy)
**Certification must be submitted*	If "Yes" Unit Packaging wgt. / No. per container	If "Yes" Package wgt. / No. per container	

3. Location of Net Contents Information	4. Size(s) Retail Container	5. Location of Label Directions
☐ Label ☐ Container		☐ On Label ☐ On labeling accompanying product

6. Manner in Which Label is Affixed to Product ☐ Lithograph ☐ Paper glued ☐ Stenciled ☐ Other _____

Section - IV

1. Contact Point *(Complete items directly below for identification of individual to be contacted, if necessary, to process this application)*

Name	Title	Telephone No. (Include Area Code)
J. Todd Frank	Regulatory Affairs Consultant	913-268-2585

Certification

I certify that the statements I have made on this form and all attachments thereto are true, accurate and complete. I acknowledge that any knowingly false or misleading statement may be punishable by fine or imprisonment or both under applicable law.

6. Date Application Received (Stamped)

2. Signature	3. Title	5. Date
J. Todd Frank	Regulatory Affairs Consultant	08/09/2013
4. Typed Name: J. Todd Frank (todd.frank@bayer.com)		

EPA Form 8570-1 (Rev. 8-94) Previous editions are obsolete White- EPA File Copy (original) Yellow- Applicant Copy

Bayer HealthCare

Via Federal Express

August 9, 2013

Document Processing Desk (NOTIF)
Office of Pesticide Programs (7504P)
U.S. Environmental Protection Agency
Room S-4900, One Potomac Yard
2777 South Crystal Drive
Arlington, VA 22202-4501

Attention: Ms. Venus Eagle/PM 01

Subject: Additional of alternate brand names:

- Advantage II Kitten (EPA Reg. No. 11556-150)
- Advantage II Small Cat (EPA Reg. No. 11556-151)
- Advantage II Large Cat (EPA Reg. No. 11556-152)

Bayer HealthCare LLC

Animal Health

P.O. Box 390
Shawnee Mission, KS
66201-0390

Dear Ms. Eagle:

Please find enclosed, for the Agency's acceptance, three Applications for Pesticide Notification, one copy of the highlighted label, and one copies of the unhighlighted labels for the subject products.

As allowed by PR Notice 98-10 Bayer HealthCare LLC Animal Health is adding Alternate Brand Names. No other changes have been made to the label.

If you have any questions, please do not hesitate to call (913-268-2585).

Sincerely,

J. Todd Frank

J. Todd Frank
Regulatory Affarirs Consultant
todd.frank@bayer.com

Enclosures:

1) Advantage II Kitten - Application w/att.
2) Advantage II Small Cat - Application w/att.
3) Advantage II Large Cat - Application w/att.

NOTIFICATION

JUL 19 2013

Reason To Issue: Addition of Alternate brand names. Date: 08/09/13
Supersedes: 02/14/13

NOTE TO REVIEWER: [(Brackets and parentheses indicate alternate language)]

[Front Panel]

Advantage® II Kitten

Alternate Brand Names:
[ExpertCare Flea Protection Kitten]
[ExpertCare Topical Flea Protection Kitten]
[ExpertCare Kitten Flea Protection]
[ExpertCare Kitten Topical Flea Protection]

Once-A-Month Topical Flea Prevention and Treatment for Cats
For Use ONLY on Cats 8 Weeks and Older and Weighing 2 – 5 lbs.

[Selected optional claims bulleted here from page 10 and/or 11]

-
-
-
-

Active Ingredients	% By Weight
Imidacloprid	9.10%
Pyriproxyfen	0.46%
Other Ingredients	90.44%
Total	100.00%

EPA Est. No. 11556-XXX-X EPA Reg No. 11556-150

KEEP OUT OF REACH OF CHILDREN

CAUTION

See back panel for Precautionary Statements.
For Directions for Use, Storage and Disposal, and First Aid see package insert inside.

[Back Panel]

Advantage® II Kitten

Once-A-Month Topical Flea Prevention and Treatment for Cats
For Use ONLY on Cats 8 Weeks and Older and Weighing 2 - 5 lbs.

READ THE ENTIRE LABEL BEFORE EACH USE
For the Prevention and Treatment of Flea Infestations

PRECAUTIONARY STATEMENTS

HAZARDS TO HUMANS

CAUTION: Harmful if swallowed. Causes moderate eye irritation. Avoid contact with eyes or clothing. Wash hands thoroughly with soap and warm water after handling. Keep out of reach of children. Do not contaminate feed or food.

HAZARDS TO DOMESTIC ANIMALS

For external use only. Do not apply to cats or kittens under 8 weeks of age or weighing less than 2 lbs. As with any product, consult your veterinarian before using this product on debilitated, aged, pregnant or nursing cats. Individual sensitivities, while rare, may occur after using ANY pesticide product for cats. If signs persist, or become more severe, consult a veterinarian immediately. If your cat is on medication, consult your veterinarian before using this or any other product.

Side Effects: Monitor your cat after application. Side effects, although very rare, may include signs of skin irritation such as redness, scratching, or other signs of discomfort. Gastrointestinal signs such as hypersalivation, vomiting or diarrhea have also been reported. If these or other side effects (such as lethargy) occur, consult your veterinarian or call 1-800-422-9874.

For consumer questions call 1-800-255-6826.
For medical emergencies call 1-800-422-9874.

RESTRICTIONS:

- Use only on cats or kittens 8 weeks and older. Do not apply to cats or kittens weighing less than 2 lbs. Do not use on other animals.

- Do not apply more than one (1) tube per treatment.
- Do not have contact or allow children to have contact with treated area until completely dry.

Net Contents: [X] Tube(s), each 0.0078 fl. oz. (0.23 mL)

[Sample - Not for (Re)Sale]

Manufactured For

Bayer HealthCare LLC
Animal Health Division
P.O. BOX 390
Shawnee Mission, Kansas 66201 USA

Made in Germany

[Back Panel and/or Insert]

Advantage® II Kitten

Once-A-Month Topical Flea Prevention and Treatment for Cats
For Use ONLY on Cats 8 Weeks and Older and Weighing 2 - 5 lbs.

READ THE ENTIRE LABEL BEFORE EACH USE
For the Prevention and Treatment of Flea Infestations

DIRECTIONS FOR USE

It is a violation of Federal Law to use this product in a manner inconsistent with its labeling.

HOW TO OPEN

[OPTION 1: INSTRUCTIONS FOR BLISTER PACK]

1. Being careful not to cut close to the blister cavities, take scissors and cut off one section of the card containing a single tube.
2. Take the separated section, and cut into the blister cavity across the small side, close to the cap of the tube.
3. Peel off the foil, and take out the tube.
4. Repeat steps 1 to 3 for each tube.

[OPTION 2: INSTRUCTIONS FOR POUCH PACK]

1. Be sure tube is at bottom of pouch.
2. Using scissors, cut the pouch across the top and remove tube.

HOW TO APPLY

1. Remove one applicator tube from the package. See "HOW TO OPEN" section.

2. Hold applicator tube in an upright position facing away from you and your pet's face and eyes. Pull cap off tube.

[Visuals Depicting How to Open Applicator Tube]

3. Turn the cap around and place other end of cap back on tube.

4. Twist cap to break seal, then remove cap from tube.

5. Part the hair on the neck at the base of the skull until the skin is visible. Place the tip of the tube on the skin and squeeze the tube to expel the entire contents directly on the skin. *Do not get this product in your cat's eyes, or allow your cat to ingest this product. The product is bitter tasting and salivation may occur for a short time if the cat licks the product immediately after treatment.* Treatment at the base of the skull will minimize the opportunity for the cat to lick the product. Do not allow the product to run off.

[Visuals Depicting Application to Animal]

6. Discard empty tube as described in Storage and Disposal.

7. Under normal conditions this product is effective for a month. However, in case of severe flea infestation, retreatment may be necessary earlier than four (4) weeks. Do not retreat more often than once every fourteen (14) days. After flea control is attained, return to a monthly retreatment schedule.

PRODUCT INFORMATION

The successive feeding activity of fleas on cats frequently elicits a hypersensitivity skin disorder known as flea allergy dermatitis (FAD) or flea bite hypersensitivity. Treatment of cats with Advantage® II Kitten kills fleas and may reduce the incidence of this condition.

Advantage® II Kitten kills the existing fleas on cats within 12 hours. Reinfesting fleas are killed within 2 hours with protection against further flea infestation lasting for up to four (4) weeks. Pre-existing pupae in the environment may continue to emerge for six (6) weeks or longer depending upon the climatic conditions.

Fleas, eggs and larvae in the cat's surroundings are killed following contact with an Advantage® II Kitten treated cat. Advantage® II Kitten provides multi-stage flea control effectively breaking all flea life-cycle stages for lasting control of flea populations.

Advantage® II Kitten kills adult fleas quickly, within 12 hours, inhibits the development of immature flea life stages and prevents them from reaching the biting adult stage.

Advantage® II Kitten is waterproof and remains effective following a shampoo treatment or after exposure to rain or sunlight.

Apply monthly treatments for optimal control and prevention of fleas.

KEEP OUT OF REACH OF CHILDREN

CAUTION

PRECAUTIONARY STATEMENTS
HAZARDS TO HUMANS

CAUTION: Harmful if swallowed. Causes moderate eye irritation. Avoid contact with eyes or clothing. Wash hands thoroughly with soap and warm water after handling. Keep out of reach of children. Do not contaminate feed or food.

FIRST AID	
If Swallowed:	• Call a poison control center or doctor immediately for treatment advice. • Have person sip a glass of water if able to swallow. • Do not induce vomiting unless told to do so by the poison control center or doctor. • Do not give anything to an unconscious person.
If In Eyes:	• Hold eye open and rinse slowly and gently with water for 15-20 minutes. Remove contact lenses, if present, after the first 5 minutes, then continue rinsing eye. • Call a poison control center or doctor for treatment advice.
If On Skin	• Wash with plenty of soap and water.
HOT LINE NUMBER	
Have the product container or label with you when calling a poison control center or doctor, or going for treatment. For medical emergencies call 1-800-422-9874. For customer questions call 1-800-255-6826.	
NOTE TO PHYSICIAN	
Treat the patient symptomatically.	

HAZARDS TO DOMESTIC ANIMALS

For external use only. Do not apply to cats or kittens under 8 weeks of age or weighing less than 2 lbs. As with any product, consult your veterinarian before using this product on debilitated, aged, pregnant or nursing cats. Individual sensitivities, while rare, may occur after using ANY pesticide product for cats. If signs persist, or become more severe, consult a veterinarian immediately. If your cat is on medication, consult your veterinarian before using this or any other product.

Side Effects: Monitor your cat after application. Side effects, although very rare, may include signs of skin irritation such as redness, scratching, or other signs of discomfort. Gastrointestinal signs such as hypersalivation, vomiting or diarrhea have also been reported. If these or other side effects (such as lethargy) occur, consult your veterinarian or call 1-800-422-9874.

For medical emergencies call 1-800-422-9874.

RESTRICTIONS:

- Use only on cats or kittens 8 weeks and older. Do not apply to cats or kittens weighing less than 2 lbs. Do not use on other animals.
- Do not apply more than one (1) tube per treatment.
- Do not have contact or allow children to have contact with treated area until completely dry.

STORAGE AND DISPOSAL

Do not contaminate water, food or feed by storage or disposal.

Pesticide Storage: Store in a cool, dry place inaccessible to children and pets. **Pesticide Disposal and Container Handling:** Nonrefillable container. **If empty**: Do not reuse or refill this container. Place in trash or offer for recycling if available. **If partly filled**: Call your local solid waste agency or 1-800-422-9874 for disposal instructions. Never place unused product down any indoor or outdoor drain.

LIMITED WARRANTY AND LIMITATION OF DAMAGES

Bayer HealthCare LLC, Animal Health Division warrants that this material conforms to the chemical description on the label. TO THE EXTENT CONSISTENT WITH APPLICABLE LAW, BAYER MAKES NO OTHER EXPRESS OR IMPLIED WARRANTY, INCLUDING ANY OTHER EXPRESS OR IMPLIED WARRANTY OF FITNESS OR MERCHANTABILITY, and no agent of Bayer is authorized to do so except in writing with a specific reference to this warranty. Any damages arising from a breach of this warranty shall be limited to direct damages and shall not include consequential commercial damages such as loss of profits or values, etc.

For more information visit www.petparents.com

[Label on Individual Tube]

Advantage® II Kitten

9.10% Imidacloprid

0.46% Pyriproxyfen

0.0078 fl. oz. (0.23 mL)

EPA Reg. No. 11556-150

Keep Out of Reach of Children

CAUTION

Read The Entire Label Before Use

BAYER

Lot No. 0000000

[OPTION 1: Label on blister card; one card containing 1, 2, 3, 4, 5, or 6 tubes]
[OPTION 2: Label on pouch containing 1 tube]

[Additional label text for OPTION 2: THIS UNIT NOT FOR RETAIL SALE]

Advantage® II Kitten

For external use only on cats and kittens 8 weeks and older and weighing 2 -5 lbs.

9.10% Imidacloprid

0.46% Pyriproxyfen

[X] - 0.0078 fl. oz. (0.23 mL) Tube(s)

EPA Reg. No. 11556-150

BAYER

NOTE TO REVIEWER: [(Brackets and parentheses indicate alternate language)]

OPTIONAL MARKETING CLAIMS [Appearing on any panel]

- For use on cats and kittens 8 weeks of age and older
- Advantage II contains [imidacloprid], [and an/the] [insect growth regulator] [IGR] [pyriproxyfen]
- A single topical application remains effective for up to [4 weeks] [a month]
- Convenient, easy-to-apply topical solution
- Convenient, easy-to-apply and fragrance free [monthly] [topical solution]
- Once a month topical flea prevention and treatment for cats 8 weeks of age or older
- Advantage II is indicated for the prevention and treatment of fleas on cats 8 weeks of age and older
- For the prevention and treatment of flea infestations
- One treatment prevents further flea infestations for up to [4 weeks] [a month]
- Kills fleas on cats within [12] hours and continues to prevent infestations for up to [four weeks] [a month]
- Kills fleas before they lay eggs
- Larval flea stages in the cat's environment are killed following contact with an Advantage II treated cat
- Kills larval stages of fleas following contact with an Advantage II treated cat
- Kills fleas within [12] hours of application
- Stops existing flea infestations by killing adult fleas
- Prevents reinfestations by killing adult fleas before they lay eggs
- Reinfesting fleas are killed within 2 hours with protection against further flea infestation
- [Prevents] [Stops] flea eggs from hatching [into biting adults]
- Effectively breaks the flea life cycle
- [Kills] [Controls] all flea life stages
- Comprehensive flea prevention and treatment
- 3-way flea protection ([kills] [controls]) adults, larvae, and eggs
- [Prevents] [Stops] flea eggs from developing into [(biting) (adult)] fleas
- Treatment with Advantage II kills fleas and may reduce the incidence of flea allergic dermatitis [FAD] or flea bite hypersensitivity
- Flea adulticide, larvicide, and ovicide
- Kills flea eggs
- Controls flea problems
- Provides flea protection
- Controls existing fleas and flea eggs plus [and] [prevents] future flea infestations
- Advantage II may be used year-round for flea [prevention][protection]

- Contains an insect growth regulator (IGR) to kill flea eggs and prevent re-infestation
- Monthly use of Advantage II kills fleas and may prevent ([flea allergy dermatitis][flea bite hypersensitivity])
- Controls existing flea infestations on your cat and prevents further infestations
- Prevents fleas on treated cats from infesting (reinfesting)
- Remains effective after bathing
- Remains effective following shampooing
- Waterproof
- Remains effective after exposure to rain or sunlight
- Fragrance-free
- In child-resistant packaging
- Starts working through contact

Material Sent for Data Extraction

Reg. # 11556-150

Description: SPOT-ON INCIDENT/~~SALES~~ DATA 6/2011 - 6/2013

☐ Material(s) Sent to Data Extraction Contractors:

- ☐ New Stamped Label Dated _____
- ☐ Notification Dated _____
- ☐ New CSF(s) Dated _____
- ☐ Other: _____

☐ Decision #: _____

☒ Other Action/Comments: SPOT-ON MITIGATION REQUIREMENTS

File this coversheet and attached materials in the jacket. It must be well organized and clipped together, NOT STAPLED. Then give the jacket with the coversheet and materials to staff in the Information Services Center (ISC) (Room S-4900). If a jacket is full or only available as an image, please file materials in a new jacket and bring it down to the (ISC). For further information please call 703-605-0716.

Reviewer: KAITLIN KELLER

Phone: 308-8172 Division: RD

Date: 6/18/2013

Bayer HealthCare

May 29, 2013

Document Processing Desk
Office of Pesticide Programs (7504P) – NonPRIA
U.S. Environmental Protection Agency
Room S-4900, One Potomac Yard
2777 South Crystal Drive
Arlington, VA 22202-4501

Attention: Ms. Venus Eagle/PM01

Bayer HealthCare LLC

Animal Health

P.O. Box 390
Shawnee Mission, KS
66201-0390

Subject: Advantage II Kitten (EPA Reg. No. 11556-150)
Advantage II Small Cat (EPA Reg. No. 11556-151)
Advantage II Large Cat (EPA Reg. No. 11556-152)
Advantage II Small Dog (EPA Reg. No. 11556-128)
Advantage II Medium Dog (EPA Reg. No. 11556-125)
Advantage II Large Dog (EPA Reg. No. 11556-127)
Advantage II Extra Large Dog (EPA Reg. No. 11556-130)

Please find enclosed a new format for the conditional registration requirement of the enhanced quarterly incident report for Advantage II Dog and Cat registrations for the quarter starting January 1, 2013.

This submission includes the following tables covering incident reporting from January 1, 2013 through March 1, 2013 by brand:

Incident Count by Severity Code and Route of Exposure: Canine, Feline, Human
Summary for ALL Species
Secondary Exposure Incident Count
Summary for ALL Species
Incident Count by Severity Code and Age
Incident Count by Severity Code and Weight
Incident Count by Breed
Summary for ALL Species
Incident Count by Clinical Sign-Summary

To provide the Agency the ability to sort, this data is being provided electronically on a CD. The data was extracted from Bayer's pharmacovigilance data base (P.V. Works).

Deaths:
Advantage II for Cats Deaths Reports with a Date First Valid between 01 Jan 2013 and 31 Mar 2013 Inclusive:

2013-US0000079
Summary:
On approximately 01-Jan-2012, a 18 year old, 16.0 pound, neutered, male, Domestic Shorthair feline, in fair condition, with a history of a urinary tract infection, was administered 1 tube of Advantage II Large Cat (Imidacloprid-Pyriproxyfen) once topically by the owner. Approximately during Feb 2012 the cat had weight loss, urinary and bowel incontinence, and vocalization. On 03-Mar-2012 the cat was examined by a veterinarian and no medical treatments were performed and the cat was euthanized.

Assessment:
The clinical signs reported are not consistent with a topically acting product. Euthanasia is never expected following the use of any topical product. No necropsy was performed and the body has already been taken care of. Without a necropsy, it is impossible to determine what other disease process played a part in the animal's death. No quality issues were noted upon product investigation.

2013-US0000716
Summary:
On an unknown date in approximately 2011, a 2 year old, 5 pound, intact, male, Domestic Shorthair feline, in good condition, with no known concomitant medical condition, was administered 1 tube of Advantage II Large Cat (Imidacloprid-Pyriproxyfen) once topically by the owner. Immediately post application the cat was tachypneic and hyperactive and the clinical signs resolved approximately **3** hours later. Did not apply the product for a period of 1 year approximately, at which time the cat was badly injured on a fence and developed a severe infection in one leg. Shortly after this, the cat was found dead. No necropsy was performed.

Assessment:
This patient died over a year following exposure to the product, and an injury resulted in a severe infection. The product was used in an off label manner and was overdosed. The signs resolved rapidly and without medical intervention. The owner originally called Bayer with questions about partial doses for Advantage II and not to report this event. Due to the medical condition that the cat developed one year after the product was applied it is unlikely that the medications played a role in the outcome of this case.

2013-US0000777
Summary:
On approximately 09-Sep-2012, a 10 year old, unknown signalment feline, in unknown condition, with no known concomitant medical condition, was administered 1 tube of Advantage II Small Cat (Imidacloprid-Pyriproxyfen) once topically by the owner. Approximately on **09** Oct 2012 the cat died. The vet was suspecting of cardiac failure.

Assessment:
Death is never expected following the use of any topical product. No necropsy was performed and the body has already been taken care of. Without a necropsy, it is impossible to determine what other disease process played a part in the animal's

death.
The owner originally called Bayer with for a different reason and not to report this event. The owner mentioned that the vet suspected of heart failure.

2013-US0001683
Summary:
On an unknown date, an 11.5 year old, 13 pound, neutered, male, Unknown Breed feline, in good condition, with no known concomitant medical conditions, was administered 1 tube of Advantage II Large Cat (Imidacloprid-Pyriproxyfen) once topically by the owner. An undetermined time after application the cat was examined by a veterinarian and diagnosed with acute renal failure. On approximately 01-Feb-2012 the cat was humanely euthanized. No necropsy was performed.

Assessment:
This is a topical acting product and would not expect to see any systemic abnormalities. This patient was diagnosed with acute renal failure and was humanely euthanized following diagnosis. Reporting party contacted BVTS exclusively to inquire about use of the product in another animal.

2013-US0002208
Summary:
On approximately 01Sep2011, a 14 year old, feline of unknown signalment, in unknown condition, with no known medical conditions, was administered 1 tube of Advantage II Small Cat (Imidacloprid-Pyriproxyfen) once topically by the owner. On approximately 01Sept2012, the cat passed away.

Assessment:
The symptom observed is not anticipated following use of this product. It is unknown what, if any, medical conditions the cat had prior to application of the product. No necropsy was performed. No quality issues were noted upon product investigation.

2013-US0002646
Summary:
On approximately 01-Jan-2012, a female, feline, of unknown signalment, in unknown condition, with no known concomitant medical conditions, was administered 1 tube of Advantage II (cat-unspecified) (Imidacloprid-Pyriproxyfen) once topically by the owner. On approximately 15-Jan-2012, the patient became pruritic. An unspecified amount of time later, the owner switched the patient to firponil / s-methoprene and the pruritus resolved. An unspecified amount of time after that, the patient died.
Assessment:
The reported signs are not anticipated following the use of this product. Numerous other factors could cause pruritus, so that should be considered.

2013-US0002929
Summary:
On approximately 01Apr2011, an 7 year old, feline of unknown signalment, in unknown condition, with no known medical conditions, was administered 1 tube of Advantage II Large Cat (Imidacloprid-Pyriproxyfen) once topically by the owner. On approximately 01Apr2012, the cat passed away, possibly from a stroke.

Assessment:
The symptoms observed are not anticipated following use of this topically-applied product. It is unknown what, if any, medical conditions, the cat had at the time the product was applied. The cat was not examined by the veterinarian and no necropsy was performed. Other etiologies must be considered. The purpose of call for the reporting party was to ask about the expiration of the product, whether or not it could be used on her new pet, and not to report the death of her previous cat. No quality issues were noted upon product investigation.

2013-US0005318
Summary:
On approximately 01Nov2012, a 15 year old, 15 pound, neutered, male, Domestic Shorthair feline, in unknown condition, with an active flea infestation was administered 1 tube of Advantage II Large Cat (Imidacloprid-Pyriproxyfen) once topically by the owner. Approximately 05Nov202 the patient developed application site alopecia. The hair grew back by approximately 26Nov2012. Approximately 18Feb2013 the patient passed away due to the development of cancer.

Assessment:
Application site alopecia may occur with any topically applied product. Considering the short time to onset and the location of the alopecia, the patient may have had an individual sensitivity to the product. The hair grew back within a few weeks without further complications. Cancer leading to death would not be typical with proper use of the topically active product. Cancer in a 15 year old pet is not uncommon. Product involvement is not likely. The intent of the phone call was to report the application site alopecia, not the death of the patient.

2013-US0005751
Summary:
On an unknown date in Sep2012 a feline of unknown signalment, in unknown condition with no known concomitant medical conditions, was administered 1 tube of Advantage II Large Cat (Imidacloprid-Pyriproxyfen) once topically by the owner. On an unknown date in Sep2012 the cat was hit by a car and subsequently died.

Assessment:
The owner initially contacted Bayer Animal Health to seek advise on how to control an active flea infestation on another pet and not to report the death of this pet. Due to patient history of being hit by a car, it is very unlikely that the product has any relation to the patient's death.

2013-US0007117
Summary:
On approximately 18Jan2013, a 2 year old, 7.5 pound, neutered, male, Domestic Longhair feline, in good condition with no known concomitant medical conditions, was administered 1 tube of Advantage II Large Cat (Imidacloprid-Pyriproxyfen) once topically by the owner. This product was used in off label manner and is considered an over dose for this patient. On approximately 28Jan2013 the cat was irritable (behavioral). On approximately 02Mar2013 the cat was regurgitating. On approximately 07Mar2013 the cat was seen by a veterinarian for abnormal breathing. On approximately 14Mar2013 the cat was seen by another veterinarian for a second opinion due to ongoing clinical signs and weight loss. Radiographs

were taken and identified fluid on the chest and abnormal appearances within the thorax, no specifics provided. On approximately 15Mar2013 the cat was having difficulty swallowing. The cat was hospitalized and fluid was drained from the chest and the cat was placed on oxygen. On 19Mar2013 the cat was not improving and was euthanized per the owner's request. A necropsy or analysis of chest fluids were not performed.

Assessment:
The product was used in an off label manner and was an over dose for this cat. Due to the long duration of the time to onset of this patient's clinical signs from when the product was used, it is very unlikely that the product has any relation to the patients illness. No necropsy was performed and the body has already been taken care of. Without a necropsy, it is impossible to determine what other disease process played a part in the animal's illness.

Advantage II for Dogs Deaths Reports with a Date First Valid between 01 Jan 2013 and 31 Mar 2013 Inclusive

2013-US0000528
Summary:
On approximately 01Jan2012, a canine of unknown signalment, in unknown condition, with no known medical conditions, was administered 1 tube of Advantage II Extra Large Dog (Imidacloprid-Pyriproxyfen) once topically by the owner. An undetermined amount of time later, the dog passed away due to old age.

Assessment:
The symptom observed is not anticipated following use of this topically-applied product. It is unknown what, if any, medical problems the dog had at the time of product application. As the owner reports the dog passed away of old age, other etiologies must be considered and product relation has been deemed unlikely. No necropsy was performed.

2013-US0000640
Summary:
On 05-Jan-2013, an 11 month old Rottweiler canine, in good condition, that was bred during her first heat cycle and currently pregnant and ready to begin whelping, was administered 1 tube of Advantage II (dog unspecified) (Imidacloprid/ Pyriproxyfen) of an unknown size once topically route by the owner. 13 hours post application the bitch began whelping at her expected delivery time. The first pup was stillborn (stillborn pup was sharing a sac with another pup) and she delivered 13 pups total within the next 5 hours. Approximately 19 hours post application, after the pups had attempted to nurse, the 12 pups began vocalizing and 6 passed away. The owner took the remaining 6 pups to the veterinarian. All of the pups had very low temperatures and were dehydrated. One of the pups presented gasping for air and was immediately given oxygen but passed away within 5 minutes. 1 of the pups was gasping and was euthanized before receiving any treatments. 1 of them received subcutaneous fluids and oxygen but passed away approximately 5 minutes later. The other 3 pups were also administered subcutaneous fluids only as they were not having any breathing issues. The remaining 3 pups were sent home with the owner. Once home, 1 of the remaining 3 nursed on the mom and then, approximately 15 minutes later, passed away. The owner has continued to bottle feed the 2 remaining pups and both of the pups and the mom are asymptomatic.

Assessment:
This is not anticipated with the proper use of a topically applied product. The veterinarian believed the cause of the events to be more likely associated with the bitch being bred at a young age during her first heat cycle. No necropsy was performed and 2 of the pups have recovered from this event with minimal veterinary intervention.

2013-US0000888
Summary:
On approximately 01-Sep-2012, a 17 year old, 45 pound, neutered, male, Border Collie canine, in fair condition, with no specific medical conditions, was administered 1 tube of Advantage II Large Dog (Imidacloprid-Pyriproxyfen) once topically by the owner. An unknown amount of time post application the dog began having difficulty walking. On approximately 30-Sep-2012 the dog was euthanized for his continued declining health. No necropsy was performed.

Assessment:
This is not expected with the proper use of the product. It is not anticipated that any signs were associated with the use of the product and the dog had never had any previous reactions with the product. This is more likely associated with the age of the dog.

2013-US0001462
Summary:
On approximately 01-Oct-2011, a 20 year old, 64 pound, spayed, female, Mixed Breed canine, in fair condition, with no known concomitant medical conditions, was administered 1 tube of Advantage II (dog-unspecified) (Imidacloprid-Pyriproxyfen) once topically by the owner. An unspecified amount of time post application the dog began having neurological signs (unspecified). The owner continued to use the product seasonally and the neurological signs continued to worsen. On 24-Oct-2012 the owner had the dog euthanized due to the condition. No necropsy was performed.

Assessment:
This is not anticipated with the proper use of the product. The dog had used the product for an extended amount of time with no issue. The dog was an elderly dog and it is impossible to determine what, if any, role the product played in these events.

2013-US0001654
Summary:
On approximately 01-Jan-2010 a 10 year old, unknown weight, spayed, female, Maltese canine, in good condition, with no known concomitant medical conditions, was administered 1 tube of Adavntage (dog unspecified) once topically by the owner. The owner continued to apply the product on an unknown basis yearly. On approximately 01-Mar-2010 the dog had difficulty breathing. The dog was examined by the veterinarian and diagnosed with chronic obstructive pulmonary disease. The veterinarian prescribed an unknown dose of prednisone and an unknown dose of theophylline at that time. These treatments were used as needed. On 07-Nov-2012 the patient was administered an unknown amount of moxidectin injectable by the attending vet. On 15-Jan-2013 the dog was administered a distemper/parvo vaccination, a lepto vaccination, and a flu vaccination by the

attending vet, and was prescribed neomycin/polymyxin B/dexamethasone drops to be applied to the eyes for conjunctivitis. The dog was also administered 1 tube of Advantage II Smal Dog (Imidacloprid-Pyrifroxyfen) once topically by the owner. On 16-Jan-2013 the dog was listless, vomiting, and had soft stool. The owner contacted the veterinarian who advised that the dog be examined but the owner declined. 2 hours later the owner contacted the veterinarian and adivsed that the dog was uncomfortable and again declined an exam. 3 hours later the owner called and advised bloody diarrhea and wanted to wait until the next morning to have her examined. On 17-Jan-2013 the dog was examined by the veterinarian. Radiographs showed a dense mass cranial to the right kidney and excess gas in the intra-intestinal area. A fecal was performed and was negative. 20 minutes later the dog collapsed with respiratory distress. The veterinarian administered .5cc of doxapram intramuscular and .3cc of epinephrine intramuscular. The dog was intubated. 5 minutes later the dog passed away. On gross necropsy performed by the veterinarian the dog was found to have hemorrhagic enteritis, an enlarged heart, and an adrenal gland tumor.

Assessment:
No quality issues were noted upon product investigation. The clinical signs are not consistent with a topically acting product. On gross necropsy the dog was found to have hemorrhagic enteritis, an enlarged heart, and an adrenal gland tumor. These are more likely to have caused the death of the patient.

2013-US0003380
Summary:
On 01-Sep-2012, a 18 year old, 10 pound*, Schnauzer/Poodle (Miniature) crossbred canine, in poor condition, with a concomitant medical condition of age related hearing loss, was administered 1 dose of Advantage II Small Dog (Imidacloprid-Pyriproxyfen) once topically by the owner. On 01 Oct 2012 the dog died of unknown causes.

Assessment:
Death is never expected following the use of any topical product. No necropsy was performed and the body has already been taken care of. Without a necropsy, it is impossible to determine what other disease process played a part in the animal's death.
The owner originally called Bayer to report an AE for a different dog and mentioned this event. The dog was 18 years old and the owner said that is death was age related.

2013-US0005133
Summary:
On approximately 01-Aug-2012, a 8 year old, 120 pound, neutered, male, Golden Retriever canine, in poor condition, with a inoperable mast cell tumor on its leg, was administered 1 tube of Advantage II (dog-unspecified) (Imidacloprid-Pyriproxyfen) once topically by the owner. The dog had been undergoing chemotherapy since approximately 01-Apr-2012. On approximately 15-Sep-2012, the mast cell tumor had increased in size and began blocking bloodflow to the leg. Euthanasia was elected by the owner and this was performed by the veterinarian. No necropsy was performed.

Assessment:
The signs exhibited by this dog are not product related, but related to its

concomitant medical condition. This dog has a mast cell tumor and was undergoing chemotherapy which was unsuccessful. The tumor had grown to a size that caused loss of blood flow to the dog's leg. The owner elected euthanasia. The caller contacted Bayer Animal Health to inquire about using the remainder of the product on their new pet and not to report this event.

2013-US0005242

Summary:

On approximately 01Aug2011, an approximately 13.5 year old, male, Chihuahua canine, in poor condition, was administered 1 tube of Advantage II (dog-unspecified) (Imidacloprid-Pyriproxyfen) once topically by the owner. Concomitant Medical Conditions: inbred; brain tumor; liver issues; epilepsy. On approximately 01Aug2012, the dog developed seizures which continued, so the owner elected to euthanize the dog.

Assessment:

The patient had numerous serious concomitant medical conditions prior to product application. The subsequent euthanasia was likely related to complications from those ongoing medical issues rather than the application of the product. Therefore, other etiologies must be considered as product involvement has been deemed unrelated.

2013-US0005257

Summary:

On 01Mar2013, an 8 year old, 8.00 pound, neutered, male, mixed breed canine, in good condition, with an active flea infestation, was administered 1 tube of Advantage II Small Dog (Imidacloprid-Pyriproxyfen) once topically by the owner. 02Mar2013 the patient was found deceased. A gross necropsy was performed and the patient was found to have an enlarged heart. No other abnormalities were noted.

Assessment:

The exact cause of death of the patient in this case was not determined. Upon necropsy examination, it was determined the patient had cardiomegaly. It is well known that cardiac disease my lead to sudden death in patients. No quality issues were noted upon product investigation. The attending veterinarian did not believe the patient's death to be related to the administration of product.

2013-US0005606

Summary:

On approximately 01-Aug-2012, a 14 year old, male, Mixed Breed canine, in unknown condition with no known concomitant medical conditions, was administered 1 tube of Advantage II Extra Large Dog (Imidacloprid-Pyriproxyfen) once topically by the owner. On 18-Dec-2012, the dog passed away at home. The owner had not applied product during the winter months. A necropsy was not performed.

Assessment:

Since limited information was provided in this event, it is unknown what, if any, role the product had in this event. Due to the 3 month duration of the time between the last product application and death, product involvement is very unlikely. No product quality issues were found in the product investigation. The initial purpose of the owner contacting Bayer animal Heath was to inquire about the use of this product for use on a different pet and not to report this event.

EPA Summary Report

Cases first valid from: 01-Jan-2013 to: 31-Mar-2013

Parameters:
For Brand : Advantage II Medium Dog

Incident Count by Severity Code and Route of Exposure

Species: Canine

		Route of Admin	
		Oral	Other
EPA Classification	D-B [Life threatening &/or resldual disabilit	*0*	*2*
	D-C [Non-life threat. pronounced symptoms	*0*	*11*
	D-D [Minimal symptoms (skin, eye or resp)	*1*	*34*
	TOTAL	**1**	**47**

Species: Feline

		Route of Admin
		Other
EPA Classification	D-D [Minimal symptoms (skin, eye or resp)	*1*
	TOTAL	**1**

Species: Human

		Route of Admin
		Other
EPA Classification	H-D [Minimal symptoms (skin, eye, or resp)	*1*
	TOTAL	**1**

Summary for ALL Species

		Route of Admin	
		Oral	Other
EPA Classification	D-A [Death]	*0*	*0*
	D-B [Life threatening &/or residual disability]	*0*	*2*
	D-C [Non-life threat. pronounced symptoms, no disability]	*0*	*11*
	D-D [Minimal symptoms (skin, eye or resp) resolved rapidly]	*1*	*35*
	D-E [Symptoms unknown or not specified]	*0*	*0*

		Route of A n	
		Oral	Other
EPA Classification	G-A [Water Contamination - see guidelines]	0	0
	G-B [Water Contamination - see guidelines]	0	0
	G-C [Water Contamination - see guidelines]	0	0
	H-A [Person Died]	0	0
	H-B [Life threat. ,repro effects, &/or residual disability]	0	0
	H-C [Non-life threat. pronounced symptoms, no disability]	0	0
	H-D [Minimal symptoms (skin, eye, or resp) resolved rapidly]	0	1
	H-E [Symptoms unknown, unspecified or "delayed or chronic"]	0	0
	ONT [Other Non-Target Organisms]	0	0
	P-A [Plant - >45% of acreage exposed]	0	0
	P-B [Plant - <45% of acreage exposed]	0	0
	PD-A [Alleged damage that could have caused human injury]	0	0
	PD-B [Alleged to have caused damage >$5,000]	0	0
	PD-C [other allegations not in PD-A or B]	0	0
	W-A [Fish or Wildlife - see EPA guidelines]	0	0
	W-B [Fish or Wildlife - see EPA guidelines]	0	0
	TOTAL	1	49

NB: Counts reflect the numbers of doses for cases with EPA products - these may differ from the number of distinct case reports.
(Data columns which return no values are suppressed).

Secondary Exposure Incident Count

Species: Feline	Incident Count
Feline	1
TOTAL	1

Species: Human	Incident Count
Human	1
TOTAL	1

Summary for all Species

	Incident Count
Feline	1
Human	1
TOTAL	2

NB: Counts reflect the number of products having secondary exposure - these may differ from the number of distinct case reports

Incident Count by Severity Code and Age

Age Category	EPA Classification				
	D-B	D-C	D-D	H-D	Unassessed
<3 months	0	0	1	0	0
3-6 months	0	0	0	0	0
6-9 months	0	0	2	0	0
9-12 months	0	0	1	0	0
1 year	0	1	1	0	0
2 years	1	0	4	0	0
3 years	0	0	5	0	0
4 years	0	0	4	0	0
5 years	0	3	4	0	0
6 years	0	1	1	0	0
7 years	0	0	4	0	0
8 years	1	1	3	0	0
9 years	0	2	2	0	0
10 years	0	1	0	0	0
11 years	0	0	1	0	0
12 years	0	1	1	0	0
13 years	0	0	0	0	0
14 years	0	0	1	0	0
15 years	0	0	0	0	0
> 15 years	0	0	0	1	0
not specified	0	1	1	0	0
TOTAL	2	11	36	1	0

NB: Counts reflect the number of patients for cases with EPA products - these may differ from the number of distinct case reports.
(Data columns which return no values are suppressed).

Incident Count by Severity Code and Weight

		EPA Classification			
		D-B	D-C	D-D	H-D
Weight Category	< 11lbs	*0*	*2*	*8*	*0*
	11 - 16lbs	*0*	*5*	*13*	*0*
	16 - 20lbs	*1*	*2*	*8*	*0*
	> 20lbs	*0*	*2*	*7*	*0*
	not specified	*1*	*0*	*0*	*1*
	TOTAL	**2**	**11**	**36**	**1**

NB: Counts reflect the number of patients for cases with EPA products - these may differ from the number of distinct case reports.
(Data columns which return no values are suppressed).

Incident Count by Breed

Species: Canine		Incident count	
Breed	Mixed Breed (Canine)	11	22%
	Chihuahua	7	14%
	Shih Tzu	6	12%
	Terrier (Jack Russell)	4	8%
	Fox Terrier	3	6%
	Poodle (Miniature)	3	6%
	Unknown Breed (Canine)	2	4%
	Cairn Terrier	1	2%
	Chinese Crested	1	2%
	Dachshund	1	2%
	Dachshund (Miniature)	1	2%
	German Shepherd Dog	1	2%
	Maltese	1	2%
	Pomeranian	1	2%
	Pug	1	2%
	Schnauzer (Miniature)	1	2%
	Terrier (Rat)	1	2%
	Yorkshire Terrier	1	2%
	Yorkshire Terrier & Poodle (Miniature)	1	2%
	TOTAL	48	100%

Species: Feline		Incident count	
Breed	Domestic Shorthair	1	100%
	TOTAL	1	100%

Species: Human		Incident count	
Breed	Unknown	1	100%
	TOTAL	1	100%

Summary for ALL Species

		Incident count	
Species	Canine	*48*	96%
	Feline	*1*	2%
	Human	*1*	2%
	TOTAL	*50*	100%

NB: Counts reflect the number of patients for cases with EPA products - these may differ from the number of distinct case reports

Incident Count by Clinical Sign - Summary

System Organ Class	Incident Count	
Skin and appendages disorders	*44*	40%
Behavioural disorders	*17*	15%
Systemic disorders	*14*	13%
Digestive tract disorders	*8*	7%
Neurological disorders	*6*	5%
Application site disorders	*4*	4%
Musculoskeletal disorders	*4*	4%
Unknown	*4*	4%
Eye disorders	*3*	3%
Respiratory tract disorders	*3*	3%
Ear and labyrinth disorders	*1*	1%
Immune system disorders	*1*	1%
Reproductive system disorders	*1*	1%
GRAND TOTAL:	*110*	

NB: Counts reflect number of signs for cases with EPA products - these may differ from the number of distinct case reports

Validation Report

EPA Summary Report

Cases first valid from: 01-Jan-2013 to: 31-Mar-2013

Parameters:
For **Brand :** Advantage II Large Dog

Incident Count by Severity Code and Route of Exposure

Species: Canine

		Route of Admin
		Other
EPA Classification	D-A [Death]	1
	D-B [Life threatening &/or residual disabilit	3
	D-C [Non-life threat, pronounced symptoms	6
	D-D [Minimal symptoms (skin, eye or resp)	26
	TOTAL	**36**

Species: Feline

		Route of Admin
		Other
EPA Classification	D-C [Non-life threat, pronounced symptoms	2
	D-D [Minimal symptoms (skin, eye or resp)	6
	TOTAL	**8**

Species: Human

		Route of Admin
		Other
EPA Classification	H-D [Minimal symptoms (skin, eye, or resp)	2
	TOTAL	**2**

Summary for ALL Species

		Route of Admin
		Other
EPA Classification	D-A [Death]	1
	D-B [Life threatening &/or residual disability]	3
	D-C [Non-life threat, pronounced symptoms, no disability]	8
	D-D [Minimal symptoms (skin, eye or resp) resolved rapidly]	32

		Route of Admin
		Other
EPA Classification	D-E [Symptoms unknown or not specified]	*0*
	G-A [Water Contamination - see guidelines]	*0*
	G-B [Water Contamination - see guidelines]	*0*
	G-C [Water Contamination - see guidelines]	*0*
	H-A [Person Died]	*0*
	H-B [Life threat. ,repro effects, &/or residual disability]	*0*
	H-C [Non-life threat. pronounced symptoms, no disability]	*0*
	H-D [Minimal symptoms (skin, eye, or resp) resolved rapidly]	*2*
	H-E [Symptoms unknown, unspecified or "delayed or chronic"]	*0*
	ONT [Other Non-Target Organisms]	*0*
	P-A [Plant - >45% of acreage exposed]	*0*
	P-B [Plant - <45% of acreage exposed]	*0*
	PD-A [Alleged damage that could have caused human injury]	*0*
	PD-B [Alleged to have caused damage >$5,000]	*0*
	PD-C [other allegations not in PD-A or B]	*0*
	W-A [Fish or Wildlife - see EPA guidelines]	*0*
	W-B [Fish or Wildlife - see EPA guidelines]	*0*
	TOTAL	**46**

NB: Counts reflect the numbers of doses for cases with EPA products - these may differ from the number of distinct case reports. (Data columns which return no values are suppressed).

Secondary Exposure Incident Count

*** No records found ***

NB: Counts reflect the number of products having secondary exposure - these may differ from the number of distinct case reports

Incident Count by Severity Code and Age

		EPA Classification					
		D-A	D-B	D-C	D-D	H-D	Unassessed
Age Category	<3 months	0	0	0	1	0	0
	3-6 months	0	0	0	2	0	0
	6-9 months	0	0	0	0	0	0
	9-12 months	0	0	0	1	0	0
	1 year	0	0	1	2	0	0
	2 years	0	1	1	2	0	0
	3 years	0	0	0	1	0	0
	4 years	0	1	2	2	0	0
	5 years	0	0	2	2	0	0
	6 years	0	0	0	2	0	0
	7 years	0	0	0	2	0	0
	8 years	0	0	0	1	0	0
	9 years	0	0	0	3	0	0
	10 years	0	0	0	2	0	0
	11 years	0	0	0	2	0	0
	12 years	0	0	0	1	0	0
	13 years	0	0	0	2	0	0
	14 years	0	1	0	2	0	0
	15 years	0	0	0	0	0	0
	> 15 years	1	0	0	0	2	0
	not specified	0	0	2	2	0	0
	TOTAL	1	3	8	32	2	0

NB: Counts reflect the number of patients for cases with EPA products - these may differ from the number of distinct case reports.
(Data columns which return no values are suppressed).

Incident Count by Severity Code and Weight

		EPA Classification				
		D-A	D-B	D-C	D-D	H-D
Weight Category	< 21lbs	*0*	*0*	*2*	*7*	*0*
	21 - 38lbs	*0*	*0*	*3*	*15*	*0*
	38 - 55lbs	*1*	*2*	*3*	*6*	*0*
	> 55lbs	*0*	*1*	*0*	*2*	*0*
	not specified	*0*	*0*	*0*	*2*	*2*
	TOTAL	1	3	8	32	2

NB: Counts reflect the number of patients for cases with EPA products - these may differ from the number of distinct case reports.
(Data columns which return no values are suppressed).

Incident Count by Breed

Species: Canine		Incident count	
Breed	Mixed Breed (Canine)	8	22%
	Pit Bull	5	13%
	Beagle	3	8%
	Bichon Frise	2	5%
	Retriever (Labrador, Black)	2	5%
	Retriever (N. Scotia Duck Tolling)	2	5%
	Unknown Breed (Canine)	2	5%
	Basset Hound	1	2%
	Border Collie	1	2%
	Bouvier Des Flandres	1	2%
	Bulldog	1	2%
	Cockapoo	1	2%
	French Bulldog	1	2%
	Pekingese	1	2%
	Poodle (Toy)	1	2%
	Schnauzer	1	2%
	Siberian Husky	1	2%
	Spaniel (Cocker)	1	2%
	Terrier (Jack Russell)	1	2%
	TOTAL	36	100%

Species: Feline		Incident count	
Breed	Domestic Shorthair	7	87%
	Siamese	1	12%
	TOTAL	8	100%

Species: Human		Incident count	
Breed	Unknown	2	100%
	TOTAL	2	100%

Summary for ALL Species

		Incident count	
Species	Canine	*36*	78%
	Feline	*8*	17%
	Human	*2*	4%
	TOTAL	*46*	100%

NB: Counts reflect the number of patients for cases with EPA products - these may differ from the number of distinct case reports

Incident Count by Clinical Sign - Summary

System Organ Class	Incident Count	
Skin and appendages disorders	*25*	26%
Systemic disorders	*15*	15%
Digestive tract disorders	*14*	14%
Behavioural disorders	*11*	11%
Application site disorders	*8*	8%
Neurological disorders	*6*	6%
Eye disorders	*5*	5%
Renal and urinary disorders	*3*	3%
Respiratory tract disorders	*3*	3%
Unknown	*3*	3%
Immune system disorders	*2*	2%
Hepato-biliary disorders	*1*	1%
Musculoskeletal disorders	*1*	1%
GRAND TOTAL:	*97*	

NB: Counts reflect number of signs for cases with EPA products - these may differ from the number of distinct case reports

Validation Report

EPA Summary Report

Cases first valid from: 01-Jan-2013 to: 31-Mar-2013

Parameters:
For Brand : Advantage II Small Dog

Incident Count by Severity Code and Route of Exposure

Species: Canine

		Route of Admin
		Other
EPA Classification	D-A [Death]	3
	D-C [Non-life threat. pronounced symptoms	4
	D-D [Minimal symptoms (skin, eye or resp)	26
	TOTAL	33

Species: Feline

		Route of Admin
		Other
EPA Classification	D-C [Non-life threat. pronounced symptoms	1
	TOTAL	1

Summary for ALL Species

		Route of Admin
		Other
EPA Classification	D-A [Death]	3
	D-B [Life threatening &/or residual disability]	0
	D-C [Non-life threat. pronounced symptoms, no disability]	5
	D-D [Minimal symptoms (skin, eye or resp) resolved rapidly]	26
	D-E [Symptoms unknown or not specified]	0
	G-A [Water Contamination - see guidelines]	0
	G-B [Water Contamination - see guidelines]	0
	G-C [Water Contamination - see guidelines]	0
	H-A [Person Died]	0

		Route of Admin
		Other
EPA Classification	H-B [Life threat. ,repro effects, &/or residual disability]	0
	H-C [Non-life threat. pronounced symptoms, no disability]	0
	H-D [Minimal symptoms (skin, eye, or resp) resolved rapidly]	0
	H-E [Symptoms unknown, unspecified or "delayed or chronic"]	0
	ONT [Other Non-Target Organisms]	0
	P-A [Plant - >45% of acreage exposed]	0
	P-B [Plant - <45% of acreage exposed]	0
	PD-A [Alleged damage that could have caused human injury]	0
	PD-B [Alleged to have caused damage >$5,000]	0
	PD-C [other allegations not in PD-A or B]	0
	W-A [Fish or Wildlife - see EPA guidelines]	0
	W-B [Fish or Wildlife - see EPA guidelines]	0
	TOTAL	**34**

NB: Counts reflect the numbers of doses for cases with EPA products - these may differ from the number of distinct case reports.
(Data columns which return no values are suppressed).

Secondary Exposure Incident Count

*** No records found ***

NB: Counts reflect the number of products having secondary exposure - these may differ from the number of distinct case reports

Incident Count by Severity Code and Age

		EPA Classification			
		D-A	D-C	D-D	Unassessed
Age Category	<3 months	0	0	0	0
	3-6 months	0	0	2	0
	6-9 months	0	2	0	0
	9-12 months	0	0	1	0
	1 year	0	0	3	0
	2 years	0	0	4	0
	3 years	0	0	3	0
	4 years	0	0	1	0
	5 years	0	0	2	0
	6 years	0	0	0	0
	7 years	0	1	2	0
	8 years	1	0	0	0
	9 years	0	0	2	0
	10 years	0	0	1	0
	11 years	0	1	2	0
	12 years	1	0	0	0
	13 years	0	0	0	0
	14 years	0	0	1	0
	15 years	0	0	0	0
	> 15 years	1	0	0	0
	not specified	0	1	2	0
	TOTAL	3	5	26	0

NB: Counts reflect the number of patients for cases with EPA products - these may differ from the number of distinct case reports.
(Data columns which return no values are suppressed).

Incident Count by Severity Code and Weight

		EPA Classification			
		D-A	D-C	D-D	Unassessed
Weight Category	< 1lbs	*0*	*0*	*0*	*0*
	1 - 5lbs	*0*	*0*	*2*	*0*
	5 - 10lbs	*1*	*2*	*17*	*0*
	> 10lbs	*1*	*2*	*6*	*0*
	not specified	*1*	*1*	*1*	*0*
	TOTAL	3	5	26	0

NB: Counts reflect the number of patients for cases with EPA products - these may differ from the number of distinct case reports.
(Data columns which return no values are suppressed).

Incident Count by Breed

Species: Canine		Incident count	
Breed	Chihuahua	10	30%
	Maltese	4	12%
	Mixed Breed (Canine)	4	12%
	Pomeranian	4	12%
	Schnauzer	2	6%
	Shih Tzu	2	6%
	Yorkshire Terrier	2	6%
	Dachshund	1	3%
	Pinscher (Miniature)	1	3%
	Terrier (Rat)	1	3%
	Unknown Breed (Canine)	1	3%
	West Highland White	1	3%
	TOTAL	33	100%

Species: Feline		Incident count	
Breed	Domestic Longhair	1	100%
	TOTAL	1	100%

Summary for ALL Species

		Incident count	
Species	Canine	33	97%
	Feline	1	3%
	TOTAL	34	100%

NB: Counts reflect the number of patients for cases with EPA products - these may differ from the number of distinct case reports

Incident Count by Clinical Sign - Summary

System Organ Class	Incident Count	
Skin and appendages disorders	32	48%
Systemic disorders	12	18%
Behavioural disorders	6	9%
Digestive tract disorders	6	9%
Eye disorders	3	4%
Respiratory tract disorders	3	4%
Cardio-vascular system disorders	2	3%
Application site disorders	1	1%
Endocrine system disorders	1	1%
Neurological disorders	1	1%
GRAND TOTAL:	67	

NB: Counts reflect number of signs for cases with EPA products - these may differ from the number of distinct case reports

Validation Report

EPA Summary Report

Cases first valid from: 01-Jan-2013 to: 31-Mar-2013

Parameters:
For Brand : Advantage II Extra Large Dog

Incident Count by Severity Code and Route of Exposure

Species: Canine

		Route of Admin
		Other
EPA Classification	D-A [Death]	2
	D-B [Life threatening &/or residual disabilit	4
	D-C [Non-life threat. pronounced symptoms	12
	D-D [Minimal symptoms (skin, eye or resp)	21
	TOTAL	**39**

Species: Feline

		Route of Admin	
		Oral	Other
EPA Classification	D-C [Non-life threat. pronounced symptoms	0	1
	D-D [Minimal symptoms (skin, eye or resp)	1	2
	TOTAL	**1**	**3**

Species: Human

		Route of Admin
		Other
EPA Classification	H-D [Minimal symptoms (skin, eye, or resp)	1
	TOTAL	**1**

Summary for ALL Species

		Route of Admin	
		Oral	Other
EPA Classification	D-A [Death]	0	2
	D-B [Life threatening &/or residual disability]	0	4
	D-C [Non-life threat. pronounced symptoms, no disability]	0	13
	D-D [Minimal symptoms (skin, eye or resp) resolved rapidly]	1	23

		Route of Adm.	
		Oral	Other
EPA Classification	D-E [Symptoms unknown or not specified]	0	0
	G-A [Water Contamination - see guidelines]	0	0
	G-B [Water Contamination - see guidelines]	0	0
	G-C [Water Contamination - see guidelines]	0	0
	H-A [Person Died]	0	0
	H-B [Life threat. ,repro effects, &/or residual disability]	0	0
	H-C [Non-life threat. pronounced symptoms, no disability]	0	0
	H-D [Minimal symptoms (skin, eye, or resp) resolved rapidly]	0	1
	H-E [Symptoms unknown, unspecified or "delayed or chronic"]	0	0
	ONT [Other Non-Target Organisms]	0	0
	P-A [Plant - >45% of acreage exposed]	0	0
	P-B [Plant - <45% of acreage exposed]	0	0
	PD-A [Alleged damage that could have caused human injury]	0	0
	PD-B [Alleged to have caused damage >$5,000]	0	0
	PD-C [other allegations not in PD-A or B]	0	0
	W-A [Fish or Wildlife - see EPA guidelines]	0	0
	W-B [Fish or Wildlife - see EPA guidelines]	0	0
	TOTAL	**1**	**43**

NB: Counts reflect the numbers of doses for cases with EPA products - these may differ from the number of distinct case reports. (Data columns which return no values are suppressed).

Secondary Exposure Incident Count

*** No records found ***

NB: Counts reflect the number of products having secondary exposure - these may differ from the number of distinct case reports

Incident Count by Severity Code and Age

		EPA Classification					
		D-A	D-B	D-C	D-D	H-D	Unassessed
Age Category	<3 months	0	0	0	0	0	0
	3-6 months	0	0	0	0	0	0
	6-9 months	0	0	0	2	0	0
	9-12 months	0	0	0	0	0	0
	1 year	0	0	0	1	0	0
	2 years	0	0	1	2	0	0
	3 years	0	1	1	2	0	0
	4 years	0	0	0	2	0	0
	5 years	0	0	3	1	0	0
	6 years	0	0	1	3	0	0
	7 years	0	1	0	1	0	0
	8 years	0	1	1	1	0	0
	9 years	0	0	0	4	0	0
	10 years	0	0	1	2	0	0
	11 years	0	1	0	2	0	0
	12 years	0	0	2	0	0	0
	13 years	0	0	0	0	0	0
	14 years	1	0	2	0	0	0
	15 years	0	0	0	1	0	0
	> 15 years	0	0	0	0	1	0
	not specified	1	0	1	0	0	0
	TOTAL	2	4	13	24	1	0

NB: Counts reflect the number of patients for cases with EPA products - these may differ from the number of distinct case reports. (Data columns which return no values are suppressed).

Incident Count by Severity Code and Weight

		EPA Classification				
		D-A	D-B	D-C	D-D	H-D
Weight Category	< 56lbs	*0*	*0*	*3*	*7*	*0*
	56 - 78lbs	*0*	*3*	*6*	*12*	*0*
	78 - 100lbs	*0*	*1*	*2*	*1*	*0*
	> 100lbs	*0*	*0*	*1*	*3*	*0*
	not specified	*2*	*0*	*1*	*1*	*1*
	TOTAL	2	4	13	24	1

NB: Counts reflect the number of patients for cases with EPA products - these may differ from the number of distinct case reports.
(Data columns which return no values are suppressed).

Incident Count by Breed

Species: Canine		Incident count	
Breed	Mixed Breed (Canine)	9	23%
	Retriever (Golden)	4	10%
	Retriever Labrador (No Description)	3	7%
	Dachshund	2	5%
	Old English Sheep Dog	2	5%
	Pit Bull	2	5%
	Rhodesian Ridgeback	2	5%
	Unknown Breed (Canine)	2	5%
	American Eskimo	1	2%
	Bloodhound	1	2%
	Boxer	1	2%
	Doberman Pinscher	1	2%
	German Shepherd Dog	1	2%
	Great Dane	1	2%
	Greyhound	1	2%
	Mastiff	1	2%
	Pinscher (Miniature)	1	2%
	Pointer (German Short-Haired)	1	2%
	Poodle (Standard)	1	2%
	Rottweiler	1	2%
	Siberian Husky	1	2%
	TOTAL	39	100%

Species: Feline		Incident count	
Breed	Domestic Longhair	2	50%
	Domestic Shorthair	1	25%
	Manx	1	25%
	TOTAL	4	100%

Species: Human		Incident count	
Breed	Unknown	*1*	100%
	TOTAL	*1*	100%

Summary for ALL Species

		Incident count	
Species	Canine	*39*	88%
	Feline	*4*	9%
	Human	*1*	2%
	TOTAL	*44*	100%

NB: Counts reflect the number of patients for cases with EPA products - these may differ from the number of distinct case reports

Incident Count by Clinical Sign - Summary

System Organ Class	Incident Count	
Skin and appendages disorders	*31*	32%
Systemic disorders	*20*	20%
Behavioural disorders	*12*	12%
Neurological disorders	*8*	8%
Digestive tract disorders	*7*	7%
Application site disorders	*5*	5%
Musculoskeletal disorders	*3*	3%
Unknown	*3*	3%
Hepato-biliary disorders	*2*	2%
Immune system disorders	*2*	2%
Respiratory tract disorders	*2*	2%
Blood and lymphatic system disorders	*1*	1%
Ear and labyrinth disorders	*1*	1%
Eye disorders	*1*	1%
GRAND TOTAL:	*98*	

NB: Counts reflect number of signs for cases with EPA products - these may differ from the number of distinct case reports

Validation Report

EP. Summary Report

Cases first valid from: 01-Jan-2013 to: 31-Mar-2013

Parameters:
For Brand : Advantage II Kitten

Incident Count by Severity Code and Route of Exposure

Species: Feline

		Route of Admin
		Other
EPA Classification	D-B [Life threatening &/or residual disabilit	1
	D-C [Non-life threat. pronounced symptoms	1
	D-D [Minimal symptoms (skin, eye or resp)	10
	TOTAL	12

Species: Rabbit

		Route of Admin
		Other
EPA Classification	D-D [Minimal symptoms (skin, eye or resp)	1
	TOTAL	1

Summary for ALL Species

		Route of Admin
		Other
EPA Classification	D-A [Death]	0
	D-B [Life threatening &/or residual disability]	1
	D-C [Non-life threat. pronounced symptoms, no disability]	1
	D-D [Minimal symptoms (skin, eye or resp) resolved rapidly]	11
	D-E [Symptoms unknown or not specified]	0
	G-A [Water Contamination - see guidelines]	0
	G-B [Water Contamination - see guidelines]	0
	G-C [Water Contamination - see guidelines]	0
	H-A [Person Died]	0

		Route of Admin
		Other
EPA Classification	H-B [Life threat. ,repro effects, &/or residual disability]	0
	H-C [Non-life threat. pronounced symptoms, no disability]	0
	H-D [Minimal symptoms (skin, eye, or resp) resolved rapidly]	0
	H-E [Symptoms unknown, unspecified or "delayed or chronic"]	0
	ONT [Other Non-Target Organisms]	0
	P-A [Plant - >45% of acreage exposed]	0
	P-B [Plant - <45% of acreage exposed]	0
	PD-A [Alleged damage that could have caused human injury]	0
	PD-B [Alleged to have caused damage >$5,000]	0
	PD-C [other allegations not in PD-A or B]	0
	W-A [Fish or Wildlife - see EPA guidelines]	0
	W-B [Fish or Wildlife - see EPA guidelines]	0
	TOTAL	13

NB: Counts reflect the numbers of doses for cases with EPA products - these may differ from the number of distinct case reports.
(Data columns which return no values are suppressed).

Secondary Exposure Incident Cou...

*** No records found ***

NB: Counts reflect the number of products having secondary exposure - these may differ from the number of distinct case reports

Incident Count by Severity Code and Age

		EPA Classification			
		D-B	D-C	D-D	Unassessed
Age Category	<3 months	0	0	2	0
	3-6 months	0	1	6	0
	6-9 months	0	0	1	0
	9-12 months	0	0	0	0
	1 year	0	0	0	0
	2 years	0	0	0	0
	3 years	0	0	0	0
	4 years	0	0	0	0
	5 years	0	0	0	0
	6 years	0	0	1	0
	7 years	0	0	0	0
	8 years	1	0	0	0
	9 years	0	0	0	0
	10 years	0	0	0	0
	11 years	0	0	0	0
	12 years	0	0	0	0
	13 years	0	0	1	0
	14 years	0	0	0	0
	15 years	0	0	0	0
	> 15 years	0	0	0	0
	not specified	0	0	0	0
	TOTAL	1	1	11	0

NB: Counts reflect the number of patients for cases with EPA products - these may differ from the number of distinct case reports.
(Data columns which return no values are suppressed).

Incident Count by Severity Code and Weight

		EPA Classification			
		D-B	D-C	D-D	Unassessed
Weight Category	< 1lbs	*0*	*0*	*0*	*0*
	1 - 2lbs	*0*	*0*	*0*	*0*
	2 - 4lbs	*0*	*0*	*4*	*0*
	> 4lbs	*1*	*1*	*3*	*0*
	not specified	*0*	*0*	*4*	*0*
	TOTAL	1	1	11	0

NB: Counts reflect the number of patients for cases with EPA products - these may differ from the number of distinct case reports.
(Data columns which return no values are suppressed).

Incident Count by Breed

Species: Feline		Incident count	
Breed	Domestic Shorthair	9	75%
	Domestic Longhair	1	8%
	Mixed Breed (Feline)	1	8%
	Tonkinese	1	8%
	TOTAL	12	100%

Species: Rabbit		Incident count	
Breed	Unknown Breed (Rabbit)	1	100%
	TOTAL	1	100%

Summary for ALL Species

		Incident count	
Species	Feline	12	92%
	Rabbit	1	8%
	TOTAL	13	100%

NB: Counts reflect the number of patients for cases with EPA products - these may differ from the number of distinct case reports

Incident Count by Clinical Sign - Summary

System Organ Class	Incident Count	
Digestive tract disorders	*6*	35%
Skin and appendages disorders	*5*	29%
Behavioural disorders	*3*	18%
Systemic disorders	*2*	12%
Application site disorders	*1*	6%
GRAND TOTAL:	*17*	

NB: Counts reflect number of signs for cases with EPA products - these may differ from the number of distinct case reports

Validation Report

EPA S[illegible]mary Report

Cases first valid from: 01-Jan-2013 to: 31-Mar-2013

Parameters:
For Brand : Advantage II Small Cat

Incident Count by Severity Code and Route of Exposure

Species: Feline

		Route of Admin
		Other
EPA Classification	D-A [Death]	2
	D-B [Life threatening &/or residual disabilit	4
	D-C [Non-life threat. pronounced symptoms	15
	D-D [Minimal symptoms (skin, eye or resp)	40
	TOTAL	61

Species: Human

		Route of Admin
		Other
EPA Classification	H-C [Non-life threat. pronounced symptoms	1
	H-D [Minimal symptoms (skin, eye, or resp)	1
	TOTAL	2

Summary for ALL Species

		Route of Admin
		Other
EPA Classification	D-A [Death]	2
	D-B [Life threatening &/or residual disability]	4
	D-C [Non-life threat. pronounced symptoms, no disability]	15
	D-D [Minimal symptoms (skin, eye or resp) resolved rapidly]	40
	D-E [Symptoms unknown or not specified]	0
	G-A [Water Contamination - see guidelines]	0
	G-B [Water Contamination - see guidelines]	0
	G-C [Water Contamination - see guidelines]	0
	H-A [Person Died]	0

		Route of Admin
		Other
EPA Classification	H-B [Life threat. ,repro effects, &/or residual disability]	0
	H-C [Non-life threat. pronounced symptoms, no disability]	1
	H-D [Minimal symptoms (skin, eye, or resp) resolved rapidly]	1
	H-E [Symptoms unknown, unspecified or "delayed or chronic"]	0
	ONT [Other Non-Target Organisms]	0
	P-A [Plant - >45% of acreage exposed]	0
	P-B [Plant - <45% of acreage exposed]	0
	PD-A [Alleged damage that could have caused human injury]	0
	PD-B [Alleged to have caused damage >$5,000]	0
	PD-C [other allegations not in PD-A or B]	0
	W-A [Fish or Wildlife - see EPA guidelines]	0
	W-B [Fish or Wildlife - see EPA guidelines]	0
	TOTAL	63

NB: Counts reflect the numbers of doses for cases with EPA products - these may differ from the number of distinct case reports. (Data columns which return no values are suppressed).

S ndary Exposure Incident Count

Species: Feline	Incident Count
Feline	1
TOTAL	1

Species: Human	Incident Count
Human	2
TOTAL	2

Summary for all Species

	Incident Count
Human	2
Feline	1
TOTAL	3

NB: Counts reflect the number of products having secondary exposure - these may differ from the number of distinct case reports

Inc ent Count by Severity Code and e

Age Category	EPA Classification						
	D-A	D-B	D-C	D-D	H-C	H-D	Unassessed
<3 months	0	0	0	0	0	0	0
3-6 months	0	0	1	1	0	0	0
6-9 months	0	1	0	6	0	0	0
9-12 months	0	0	0	4	0	0	0
1 year	0	1	3	1	0	0	0
2 years	0	1	2	2	0	0	0
3 years	0	0	0	3	0	0	0
4 years	0	0	2	4	0	0	0
5 years	0	0	3	3	1	0	0
6 years	0	0	0	1	0	0	0
7 years	0	0	0	3	0	0	0
8 years	0	0	1	1	0	0	0
9 years	0	0	0	0	0	0	0
10 years	1	0	0	1	0	0	0
11 years	0	0	0	0	0	0	0
12 years	0	0	0	0	0	0	0
13 years	0	0	1	2	0	0	0
14 years	1	0	0	0	0	0	0
15 years	0	1	0	4	0	0	0
> 15 years	0	0	1	1	0	1	0
not specified	0	0	1	3	0	0	0
TOTAL	2	4	15	40	1	1	0

NB: Counts reflect the number of patients for cases with EPA products - these may differ from the number of distinct case reports.
(Data columns which return no values are suppressed).

Incide Count by Severity Code and We it

		EPA Classification					
		D-A	D-B	D-C	D-D	H-C	H-D
Weight Category	< 5lbs	0	0	1	0	0	0
	5 - 7lbs	0	1	5	11	0	0
	7 - 9lbs	0	2	1	9	0	0
	> 9lbs	0	0	7	16	0	0
	not specified	2	1	1	4	1	1
	TOTAL	2	4	15	40	1	1

NB: Counts reflect the number of patients for cases with EPA products - these may differ from the number of distinct case reports.
(Data columns which return no values are suppressed).

Incident Count by Breed

Species: Feline		Incident count	
Breed	Domestic Shorthair	34	55%
	Domestic Longhair	8	13%
	Siamese	5	8%
	Unknown Breed (Feline)	4	6%
	Domestic Mediumhair	3	4%
	Abyssinian	2	3%
	Persian	2	3%
	American Shorthair	1	1%
	Mixed Breed (Feline)	1	1%
	Ragdoll	1	1%
	TOTAL	61	100%

Species: Human		Incident count	
Breed	Unknown	2	100%
	TOTAL	2	100%

Summary for ALL Species

		Incident count	
Species	Feline	61	96%
	Human	2	3%
	TOTAL	63	100%

NB: Counts reflect the number of patients for cases with EPA products - these may differ from the number of distinct case reports

Inci[illegible]it Count by Clinical Sign - Summ[illegible]y

System Organ Class	Incident Count	
Skin and appendages disorders	*37*	28%
Systemic disorders	*27*	20%
Behavioural disorders	*18*	14%
Digestive tract disorders	*18*	14%
Neurological disorders	*12*	9%
Application site disorders	*8*	6%
Unknown	*5*	4%
Blood and lymphatic system disorders	*3*	2%
Respiratory tract disorders	*2*	2%
Ear and labyrinth disorders	*1*	1%
Eye disorders	*1*	1%
Immune system disorders	*1*	1%
GRAND TOTAL:	*133*	

NB: Counts reflect number of signs for cases with EPA products - these may differ from the number of distinct case reports

Validation Report

EPA S[illegible]mary Report

Cases first valid from: 01-Jan-2013 to: 31-Mar-2013

Parameters:
For Brand : Advantage II Large Cat

Incident Count by Severity Code and Route of Exposure

Species: Feline

		Route of Admin
		Other
EPA Classification	D-A [Death]	7
	D-B [Life threatening &/or residual disabilit	12
	D-C [Non-life threat. pronounced symptoms	37
	D-D [Minimal symptoms (skin, eye or resp)	140
	TOTAL	**196**

Species: Human

		Route of Admin
		Other
EPA Classification	H-C [Non-life threat. pronounced symptoms	3
	H-D [Minimal symptoms (skin, eye, or resp)	3
	TOTAL	**6**

Summary for ALL Species

		Route of Admin
		Other
EPA Classification	D-A [Death]	7
	D-B [Life threatening &/or residual disability]	12
	D-C [Non-life threat. pronounced symptoms, no disability]	37
	D-D [Minimal symptoms (skin, eye or resp) resolved rapidly]	140
	D-E [Symptoms unknown or not specified]	0
	G-A [Water Contamination - see guidelines]	0
	G-B [Water Contamination - see guidelines]	0
	G-C [Water Contamination - see guidelines]	0
	H-A [Person Died]	0

		Route of Admin
		Other
EPA Classification	H-B [Life threat. ,repro effects, &/or residual disability]	0
	H-C [Non-life threat. pronounced symptoms, no disability]	3
	H-D [Minimal symptoms (skin, eye, or resp) resolved rapidly]	3
	H-E [Symptoms unknown, unspecified or "delayed or chronic"]	0
	ONT [Other Non-Target Organisms]	0
	P-A [Plant - >45% of acreage exposed]	0
	P-B [Plant - <45% of acreage exposed]	0
	PD-A [Alleged damage that could have caused human injury]	0
	PD-B [Alleged to have caused damage >$5,000]	0
	PD-C [other allegations not in PD-A or B]	0
	W-A [Fish or Wildlife - see EPA guidelines]	0
	W-B [Fish or Wildlife - see EPA guidelines]	0
	TOTAL	**202**

NB: Counts reflect the numbers of doses for cases with EPA products - these may differ from the number of distinct case reports. (Data columns which return no values are suppressed).

S ondary Exposure Incident Coun

Species: Human	Incident Count
Human	3
TOTAL	3

Summary for all Species

	Incident Count
Human	3
TOTAL	3

NB: Counts reflect the number of products having secondary exposure - these may differ from the number of distinct case reports

Incid t Count by Severity Code and Ag

Age Category	EPA Classification						
	D-A	D-B	D-C	D-D	H-C	H-D	Unassessed
<3 months	0	0	0	0	0	0	0
3-6 months	0	1	0	2	0	0	0
6-9 months	0	0	1	2	0	0	0
9-12 months	0	0	0	8	0	0	0
1 year	0	2	3	16	0	0	0
2 years	2	0	5	14	0	0	0
3 years	0	0	1	8	0	0	0
4 years	0	0	2	10	0	0	0
5 years	0	0	3	10	0	0	0
6 years	0	1	3	11	0	0	0
7 years	1	1	4	7	0	0	0
8 years	0	2	0	5	0	0	0
9 years	0	1	4	7	0	0	0
10 years	0	0	0	10	0	0	0
11 years	1	1	3	6	0	0	0
12 years	0	2	1	4	0	0	0
13 years	0	0	2	6	0	0	0
14 years	0	1	2	2	0	0	0
15 years	1	0	2	0	0	0	0
> 15 years	1	0	1	4	2	1	0
not specified	1	0	0	8	1	2	0
TOTAL	7	12	37	140	3	3	0

NB: Counts reflect the number of patients for cases with EPA products - these may differ from the number of distinct case reports.
(Data columns which return no values are suppressed).

Incid[illegible]t Count by Severity Code and W[illegible]ht

		EPA Classification					
		D-A	D-B	D-C	D-D	H-C	H-D
Weight Category	< 9lbs	2	0	2	12	0	0
	9 - 14lbs	1	3	23	83	0	0
	14 - 20lbs	2	8	7	24	0	0
	> 20lbs	0	0	2	13	1	0
	not specified	2	1	3	8	2	3
	TOTAL	7	12	37	140	3	3

NB: Counts reflect the number of patients for cases with EPA products - these may differ from the number of distinct case reports.
(Data columns which return no values are suppressed).

Incident Count by Breed

Species: Feline		Incident count	
Breed	Domestic Shorthair	112	57%
	Domestic Longhair	35	17%
	Unknown Breed (Feline)	11	5%
	Domestic Mediumhair	9	4%
	Persian	5	2%
	Maine Coon Cat	4	2%
	American Shorthair	3	1%
	Burmese	3	1%
	Russian Blue	3	1%
	Bengal	2	1%
	Manx	2	1%
	Ragdoll	2	1%
	Siamese	2	1%
	Calico	1	0%
	Devon Rex	1	0%
	Tonkinese	1	0%
	TOTAL	196	100%

Species: Human		Incident count	
Breed	Unknown	6	100%
	TOTAL	6	100%

Summary for ALL Species

		Incident count	
Species	Feline	196	97%
	Human	6	3%
	TOTAL	202	100%

NB: Counts reflect the number of patients for cases with EPA products - these may differ from the number of distinct case reports

Incident Count by Clinical Sign - Summary

System Organ Class	Incident Count	
Application site disorders	***74***	19%
Skin and appendages disorders	***67***	17%
Systemic disorders	***67***	17%
Behavioural disorders	***58***	15%
Digestive tract disorders	***56***	15%
Neurological disorders	***28***	7%
Renal and urinary disorders	***9***	2%
Eye disorders	***8***	2%
Respiratory tract disorders	***8***	2%
Ear and labyrinth disorders	***6***	2%
Unknown	***4***	1%
Endocrine system disorders	***1***	0%
GRAND TOTAL:	***386***	

NB: Counts reflect number of signs for cases with EPA products - these may differ from the number of distinct case reports

Validation Report

Bayer HealthCare
Animal Health

November 28, 2012

Document Processing Desk
Office of Pesticide Programs (7504P) – NonPRIA
U.S. Environmental Protection Agency
Room S-4900, One Potomac Yard
2777 South Crystal Drive
Arlington, VA 22202-4501

Attention: Ms. Venus Eagle/PM01

Subject: Advantage II Kitten (EPA Reg. No. 11556-150)
Advantage II Small Cat (EPA Reg. No. 11556-151)
Advantage II Large Cat (EPA Reg. No. 11556-152)
Advantage II Small Dog (EPA Reg. No. 11556-128)
Advantage II Medium Dog (EPA Reg. No. 11556-125)
Advantage II Large Dog (EPA Reg. No. 11556-127)
Advantage II Extra Large Dog (EPA Reg. No. 11556-130)

Bayer HealthCare LLC
Animal Health
P.O. Box 390
Shawnee Mission, KS 66201-0390

Please find enclosed the conditional registration requirement of enhanced quarterly incident report for Advantage II Dog and Cat registrations for the quarter starting July 1, 2012.

This submission includes the following tables covering incident reporting from July 1, 2012 through September 30, 2012:

Summary Table (multiple pages due to length)
Breed Summary
Age Range Summary
Clinical Signs Summary
Organ System Summary
Patient Weight Range Summary
Product Weight Range Summary
Route of Exposure Summary
Secondary Exposure Summary

Due to the length of some of the tables and to provide the Agency the ability to sort, this data is being provided electronically on a CD. The data was extracted from Bayer's pharmacovigilance data base (P.V. Works).

Deaths:

Advantage II for Cats Deaths for Reports with a Date First Valid between 01 Jul 2012 and 30 Sep 2012 Inclusive

*Included in the Summaries are reports not factored into statistical analysis as the products were for Advantage II (unspecified).

2012-US0028623

Summary:

Due to the sensitive nature of the situation, specifics of this event are unknown, therefore this was reported as such. On approximately 20-Jun-2012, an unknown old, Unknown Breed feline, in unknown condition, was administered 1 tube of Advantage II Small Cat (Imidacloprid-Pyriproxyfen) once topically by the owner. The cat has no known concomitant medical conditions. On approximately 01-Jul-2012 the cat died due to an unknown cause.

Assessment:

Death is never expected following the application of Advantage II. The product is safe and non-toxic and the cause of death is unknown. The owner called to ask questions regarding flea treatment for her cats and dogs and mentioned the one of her cats died recently.

2012-US0029001

Summary:

On approximately 01-May-2012, a 7 pound, female, Unknown Breed feline, in poor condition, was administered 1 tube of Advantage II Large Cat (Imidacloprid-Pyriproxyfen) once topically by the owner. The cat had a kidney mass. On 29-May-2012 the cat died. After death there was a palpable mass on the cat's kidneys.

Assessment:

Death is never expected following the application of a topical product. Without further information, it is unknown what, if any, role the product could have had in this event. The cat's owner called for information on another product and mentioned during the phone call that this cat had passed away.

2012-US0029321

Summary:

On 11Jul2012, a 2 year old, 8 pound, spayed, female, Domestic Shorthair feline, in good condition, with no known concomitant medical conditions, was administered 1 tube of Advantage II Small Cat (Imidacloprid-Pyriproxyfen) once topically by the owner. 12Jul2012 the patient was found deceased. No necropsy was able to be performed as the patient's remains had already been disposed of.

Assessment:

Death would not be expected with proper use of this topically active product. No necropsy was able to be performed. Therefore the cause of death cannot be determined.

What role, if any, the product played in this case can also not be determined. No quality issues were noted upon product investigation.

2012-US0030966

Summary:

On approximately 20-Jul-2012, a 2 year old, 5.70 pound, male, Domestic Shorthair feline, in good condition, with no known concomitant medical conditions, was administered 1 tube of Advantage II Small Cat (Imidacloprid-Pyriproxyfen) once topically by the owner. Approximately 1.5 hours post application, the cat was ataxic (could not walk and unable to stand because he is falling over), had mydriasis, was vocalizing, and was laying in an abnormal area in the home (behavioral). On 22-Jul-2012 the cat passed away. The case is being reported with minimal information. Unsuccessful contact attempts have been made to obtain more information.

Assessment:

The clinical signs exhibited prior to the death of the patient are not indicative of intoxication with either of the active ingredients. The cause of death is unknown despite attempts to obtain further information. What role, if any, the product played in this case cannot be determined.

2012-US0030977

Summary:

On 20Jul2012, an 8 year old, 11.00 pound, male, Domestic Shorthair feline, in good condition, with no known concomitant medical conditions, was administered 1 tube of Advantage II Large Cat (Imidacloprid-Pyriproxyfen) once topically by the owner. At the same time, a dog in the house also had K9 Advantix II Extra Large Dog applied. On 21Jul2012 (Approximately 7.5 hours post application) the patient developed ataxia and began panting. The patient was evaluated by a veterinarian and unknown treatments were performed. The patient's signs progressed into seizures and it was decided to euthanize the patient on an unspecified date.

Assessment:

Clinical signs and outcome of this nature are not known to occur to imidacloprid or pyriproxyfen. A specific diagnosis for the clinical signs exhibited could not be provided.

2012-US0033328

Summary:

On 14-May-2012, a 12 year old, 12 pound, neutered, male, Domestic Shorthair feline, in fair condition, with diabetes mellitus and rash, was administered 1 tube of Advantage II Large Cat (Imidacloprid-Pyriproxyfen) once topically by the owner. The diabetes is controlled with twice daily insulin. The cat was fine after application of the product and had used the product the prior 2 months with no issues. Owner stated that the tubes seemed to have more liquid in them. On 28-May-2012 two weeks post application of the product, the cat passed away. No necropsy was performed.

Assessment:
No necropsy was performed and the body has already been taken care of. Without a necropsy, it is impossible to determine what other disease process played a part in the animal's death. No quality issues were noted upon product investigation.

2012-US0034319

Summary:
On an unknown date, a 15 year old, feline, whose age, weight, and condition are unknown, was administered 1 tube of Advantage II Small Cat (Imidacloprid-Pyriproxyfen) once topically by the owner. At an undetermined time after application the patient developed a thyroid condition and was subsequently euthanized on an unknown date. Due to the nature of the communication, more specific information could not be obtained; the case will be reported with the limited information available.

Assessment:
Thyroid disease would not be expected after proper use of this topically active product. The patient was elderly and thyroid disease is no uncommon in elderly cats. Product involvement is unlikely. The patient was then subsequently euthanized due to its condition. No quality issues were noted upon product investigation.

2012-US0035252

Summary:
On 22-Jul-2012, a 4 year old, 10 pound, spayed, female, Domestic Shorthair feline, in fair condition, with an active flea infestation and a lower urinary tract disease, was administered 1 tube of Advantage II Large Cat (Imidacloprid-Pyriproxyfen) once topically by the owner. The cat was also bathed several times in an unknown flea shampoo and was administered a flea dip product. On 25-Jul-2012 the cat received an additional dose of Advantage II. On approximately 28-Aug-2012 the cat died. No necropsy was performed.

Assessment:
The clinical sign reported is not consistent with a topically acting product. Death is never expected following the use of any topical product. No necropsy was performed and the body has already been taken care of. Without a necropsy, it is impossible to determine what other disease process played a part in the animal's death.

2012-US0037573

Summary:
The cat was started on an unknown dose of prednisolone orally on approximately 01Aug2010. On 25Jul2012, a 15 year old, 6.5 pound, spayed, female, Domestic Shorthair, in fair condition, with a history of intestinal lymphoma, was administered 1 tube of Advantage II Small Cat (Imidacloprid-Pyriproxyfen) once topically by the owner. An undetermined amount of time later, the cat developed lameness in her hind legs. The owner declined diagnostics and treatments for the cat and elected to euthanize the cat on approximately 09Aug2012.

Assessment:
The symptom reported is not anticipated following use of this topically-applied product. It should be noted that the cat had intestinal lymphoma prior to product application. It is likely that the symptom observed was a result of that pre-existing condition, rather than related to the product. The owner elected to euthanize the cat.

2012-US0038107
Summary:
On 25-Aug-2012, an 11 year old, 9.1 pound, spayed, female, Persian feline, in fair condition, with a recent change in behavior (hiding) and flea infestation, was administered 1 tube of Advantage II Large Cat (Imidacloprid-Pyriproxyfen) once topically by the owner. 4 hours post application the cat had hind limb weakness. The cat was not seen or treated by a veterinarian. 8 hours post application the cat passed away. No necropsy was performed.

Assessment:
This is not anticipated with the proper use of the product. It is unknown what, if any, role the product played in this event. This cat had recently begun behaving abnormally, therefore, other etiologies should be considered. No necropsy examination was performed, therefore the exact cause of death cannot be determined.

2012-US0038281
Summary:
On 02-Jul-2012, a 2 year old, 8 pound, spayed, female, Domestic Mediumhair feline, in good condition, with no known concomitant medical conditions, was administered 1 tube of Advantage II Small Cat (Imidacloprid-Pyriproxyfen) once topically by the owner. On 08-Jul-2012 the pet developed respiratory distress and was examined by a veterinarian. Unknown procedures were performed and the pet was euthanized. No necropsy examination was performed.

Assessment:
The clinical sign reported is not consistent with a topically acting product. Death is never expected following the use of any topical product. No necropsy was performed and the body has already been taken care of. Without a necropsy, it is impossible to determine what other disease process played a part in the animal's death. No quality issues were noted upon product investigation.

2012-US0039042
Summary:
Due to the specifics of this case being unknown, some aspects were approximated and the case is reported as such. On approximately 01-Jul-2012, a 15 year old, Mixed Breed feline, in poor condition, with diabetes mellitus, was administered 1 tube of Advantage II Large Cat (Imidacloprid-Pyriproxyfen) once topically by the owner. On an undetermined date following the application of product the cat died due to its diabetes.

Assessment:
This feline was reported to have diabetes mellitus and died due to complications of its disease. Advantage is a safe, non-toxic product and signs of this nature would not be anticipated. The owner called to see if product could be used on her new pet and not because product caused a problem.

2012-US0039233
Summary:
On approximately 01Aug2011, a feline of unknown signalment, in unknown condition, with no known medical conditions, was administered 1 tube of Advantage II Small Cat (Imidacloprid-Pyriproxyfen) once topically by the owner. An undetermined amount of time later, the cat was euthanized. No other information was provided by the reporting party at the time of the phone call.

Assessment:
The intent of the phone call to Bayer was to ask about dosing another cat with the product and not to report the death of this patient. The product continues to be used in this home. A product investigation did not reveal any product quality issues.

2012-US0040230
Summary:
On approximately 01-Aug-2011, a 20 year old, Unknown Breed feline, in unknown condition, with no known concomitant medical conditions, was administered 1 tube of Advantage II Small Cat (Imidacloprid-Pyriproxyfen) once topically by the owner. An unknown day in January 2012 the cat was found deceased.

Assessment:
Death is never an expected outcome after the use of Advantage II. The cat was geriatric and there could have been many other contributing factors in this cat's death. Also, the death of the cat occurred several months after the last application of product. The owner called with questions regarding treatment of a new cat and mentioned that this cat was deceased.

2012-US0041358
Summary:
On 23-Aug-2012, a 5 week old, 1.4 pound, intact, male, Domestic Shorthair feline, in unknown condition, with a concomitant medical condition of a severe flea infestation, was administered 1 tube of Advantage II Kitten (Imidacloprid-Pyriproxyfen) once topically by the owner. This is an extra-label use of the product per the patient weight. On 25-Aug-2012, the patient died from anemia.

Assessment:
This product was used in an off-label manner as the patient was only 5 weeks old. Even though this was off-label, we still would not expect death after product use due to this

being a topically active product. The patient had a heavy flea infestation, which should be considered as a potential cause.

2012-US0041813

Summary:

On 08Sep2012, a 3 year old, 8 pound, male, Domestic Shorthair feline, in good condition, was administered 1 tube of Advantage II Large Cat (Imidacloprid-Pyriproxyfen) once topically by the owner. This is an overdose of the product. Within several minutes post application the patient began hypersalivating. Hypersalivation lasted approximately 3-4 hours and resolved. 10Sep2012 the patient seemed to be in pain when walking. 11Sep2012 the patient became lethargic and then was unable to be found for a few days until he was found deceased in their home on 13Sep2012. No necropsy was performed.

Assessment:

The product was used in an off label manner. The patient was given an overdose. The product has a wide margin of safety and death after use of this topically active product would not be anticipated. Death could have multiple potential causes and other etiologies cannot be ruled out. A necropsy was not performed therefore the cause of death is unable to be determined.

2012-US0042064

Summary:

On approximately 10-Jul-2012, a 8 year old, 16 pound, neutered, male, Maine Coon Cat feline, in poor condition, with concomitant medical conditions of hypertrophic cardiomyopathy and a saddle thrombus, was administered 1 tube of Advantage II Large Cat (Imidacloprid-Pyriproxyfen) once topically by the owner. Immediately after application, the patient began to "go nuts" (behavioral). On approximately 17-Jul-2012, the patient was euthanized due to the saddle thrombus.

Assessment:

The symptom reported is not anticipated following the use of this product. The patient may have been exhibiting a behavioral response to having a liquid product applied. The patient had serious concomitant illnesses and was euthanized due to the saddle thrombus. The initial contact to Bayer was to ask questions about her other cat and not to report the death of this patient.

2012-US0043484

Summary:

On approximately 01-Jul-2012, a 16 year old, unknown signalment, Domestic Shorthair feline, in unknown condition, with a concomitant medical condition of anorexia, was administered 1 tube of Advantage II Large Cat (Imidacloprid-Pyriproxyfen) once topically by the owner. On approximately 15 Jul 2012 the cat was euthanaized due to being anorexic.

Assessment:
The clinical sign reported is not consistent with a topically acting product. Death is never expected following the use of any topical product. No necropsy was performed and the body has already been taken care of. Without a necropsy, it is impossible to determine what other disease process played a part in the animal's death. The caller originally called to ask a question about our product and mentioned the cat that was euthanized.

Advantage II for Dogs Deaths for Reports with a Date First Valid between 01 Jul 2012 and 30 Sep 2012 Inclusive

*Included in the Summaries are reports not factored into statistical analysis as the products were for Advantix II (unspecified).

2012-US0028195
Summary:
Due to the nature of the communication, more specific information could not be obtained; the case will be reported with the limited information available. On an unknown date, a 17 year old, spayed female, Labrador Retriever canine, in unknown condition, with no known concomitant medical conditions, was administered 1 tube of Advantage II (dog-unspecified) (Imidacloprid-Pyriproxyfen) once topically by the owner. An unspecified amount of time after the product was applied the dog passed away from old age. No necropsy was performed.

Assessment:
The intent of the phone call to Bayer Animal Health was not to report the death of this patient and was mentioned in passing. This patient was 17 years old and died of old age. The owner did not feel the product had any relation in the pets' death and is continuing to use the product on a new pet.

2012-US0028723
Summary:
On approximately 01-Apr-2012, a 12 year old, female, Basset Hound canine, in fair condition, was administered 1 tube of Advantage II Extra Large Dog (Imidacloprid-Pyriproxyfen) once topically by the owner. The dog was diagnosed with a tumor in her mouth. The dog died on approximately 15-Apr-2012.

Assessment:
Death is never an expected outcome with the use of a topical product. The dog was diagnosed with a tumor in his mouth and the death is more than likely due to this. The caller was given three tubes of product from this dog's owner and was calling to find out if they could be used. It was only mentioned in passing that this patient was deceased.

2012-US0029680

Summary:

On approximately 01Jul2011, a canine of unknown signalment, in unknown condition, with no known medical conditions, was administered 1 tube of Advantage II Medium Dog (Imidacloprid-Pyriproxyfen) once topically by the owner.

An undetermined amount of time later, the dog passed away. No other information was provided by the reporting party.

Assessment:

The symptom reported is not anticipated following the use of this topically-applied product. No previous medical history on the dog was provided. It is unknown what, if any, medical conditions the dog had at the time the product was applied. Therefore, other etiologies must be considered. The intent of the call to Bayer was to ask if the remaining product could be used on a new pet, and not to report the death of the patient or any adversity with the product.

2012-US0030637

Summary:

On 04-Jul-2012, a 12 year old, 41 pound, neutered, male, Chowchow canine, in unknown condition, with a history of fleas and had not been seen by the veterinarian for 6 years, was administered 1 tube of Advantage II Large Dog (Imidacloprid-Pyriproxyfen) once topically by the owner. Product was applied entirely at one area at the base of the neck. On 9-Jul-2012 pet developed hair loss at the application site on the neck and on the caudodorsum. On 10-Jul-2012 skin lesions developed in the affected areas of hair loss. This developed into necrotic tissue on approximately 11-Jul-2012. On 13-Jul-2012 the dog was examined by a veterinarian, and prescribed Cephalexin 500mg twice daily and silversulfasalazine topical cream. On 18-Jul-2012 the patient was re-examined and prescribed prednisone 20mg one time daily on a decreasing dose. 21-Jul-2012 this patient passed away. No necropsy was performed.

Assessment:

This dog had not been seen by the veterinarian for the past 6 years, therefore the state of its medical health was unknown. Other etiologies should be considered. The cause of the necrotic skin at the application site was not determined. The extent of the clinical signs reported and ultimate outcome of this patient is not fitting with the properties of the product. No necropsy was performed therefore the exact cause of death is unknown.

2012-US0032371

Summary:

On 16Jul2012, an 8 year old, 54.7 pound, intact, male, Labrador Retriever crossbred canine, in good condition, with no known medical conditions, was administered the following vaccines: Rabies, Distemper, and Bordetella. A heartworm test was negative (normal). On 17Jul2012, the dog was administered 1 tablet of milbemycin oxime once orally by the owner. On 18Jul2012, the dog was administered 1 tablet of acepromazine maleate once orally by the owner. After that, the dog received 1 tube of Advantage II

Large Dog (Imidacloprid-Pyriproxyfen) once topically by the owner. Several hours later, the dog passed away.

Assessment:
This patient received multiple medications prior to administration of Advantage II. The medical condition for which the acepromazine was administered is unknown. No necropsy results are available to determine the cause of death. No quality issues were noted upon product investigation. What role, if any, the product played in this case cannot be determined.

2012-US0035651
Summary:
On 01-Feb-2012, a 13 year old, 50 pound, male, Golden Retriever Mix canine, in poor condition, was administered 1 tube of Advantage II Large Dog (Imidacloprid-Pyriproxyfen) once topically by the owner. The dog has a history of renal insufficiency and was on dialysis. On 15-May-2012 the dog had a severe seizure. The owner presented the dog to the veterinarian and euthanasia was elected.

Assessment:
Death is never an expected outcome from a topically applied product. The dog had a history of renal failure and when the dog had a severe seizure the owners elected euthanasia. The owner called only to ask if this box of product could be used on another dog that she has.

2012-US0036285
Summary:
On 15-Jul-2012, a 10 year old, 75 pound, spayed, female, English Bulldog canine, in good condition, with a history of entropion and bladder stones, was administered 1 tube of Advantage II Extra Large Dog (Imidacloprid-Pyriproxyfen) once topically by the owner. Approximately 3 hours after application of the product the dog began vomiting. One hour after that the dog stood up and died. A necropsy was not performed.

Assessment:
Death is never an expected outcome from the application of a topical product. No necropsy was performed so cause of death could not be determined. This product is safe and non-toxic and death would not be anticipated. The initial call into Bayer Animal Health was to inquire about using the product on a new pet and not to report the death of this pet.

2012-US0036376
Summary:
On an unknown date approximately March 2011, a 11 year old, 92 pound, neutered, male, Retriever Labrador (No Description)/Rottweiler crossbred canine, in good condition, with no known concomitant medical conditions, was administered 1 tube of Advantage II (dog-unspecified) (Imidacloprid-Pyriproxyfen) once topically by the owner.

On 11-Jun-2012 the dog passed away due to old age. No treatments were performed. The dog was not seen by a veterinarian. No necropsy was performed.

Assessment:
The owner initially contacted Bayer Animal Health to seek advice on how to control an active flea infestation and not to report the death of this pet. Due to the long duration of the time to onset of this patient's death from when the product was used, it is very unlikely that the product has any relation to the patient's death. No necropsy was performed so it is impossible to determine the exact cause of death.

2012-US0036378
Summary:
On an unspecified date approximately May-2012, a 7.5 year old, 134 pound, intact, male, Rottweiler canine, in good condition, with no known concomitant medical conditions, was administered 1 tube of Advantage II (dog-unspecified) (Imidacloprid-Pyriproxyfen) once topically by the owner. On 13-Jul-2012 the dog passed away, presumably, from a blood clot. It is unknown if the dog was seen or treated by a veterinarian. No necropsy was performed.

Assessment:
The owner initially contacted Bayer Animal Health to seek advise on how to control an active flea infestation and not to report the death of this pet. Due to the long duration of the time to onset of this patient's death from when the product was used, it is very unlikely that the product has any relation to the patient's death. No necropsy was performed so the exact cause of death is unknown.

2012-US0036472
Summary:
On 01-Jun-2012, a 9 year old, 85 pound, intact, male, Pit Bull canine, in poor condition, with a known medical history of heart worms, was administered 1 tube of Advantage II Extra Large Dog (Imidacloprid-Pyriproxyfen) once topically by the owner. On 22-Jun-2012 the pet passed away.

Assessment:
Due to the concomitant medical conditions of heart worm disease that this pet was diagnosed with, it is unlikely that a topically acting product was related to the death of the patient.

2012-US0037452
Summary:
On approximately 07Aug2012, a 9 year old, 8 pound, female, Miniature Pinscher, in good condition, with no known medical conditions, was administered 1 tube of Advantage II Small Dog (Imidacloprid-Pyriproxyfen) once topically by the owner. That night, the dog slept in bed with the owner. The morning of 08Aug2012, the dog was unable to walk and her whole body was shaking. The owner bathed the dog with an herbal shampoo. The dog was seen at the veterinary clinic and sent home with pain pills

and anti-inflammatory pills. The symptoms continued. The owner declined any other diagnostics and treatments for the dog and elected to euthanize her on approximately 24Aug2012.

Assessment:
The symptom observed is not anticipated following the use of this topically-applied product. It should be noted that the dog was a dachshund; it is not unusual for dachshunds to experience back injuries. No quality issues were noted upon product investigation. The owner declined diagnostics and treatments and elected to euthanize the dog instead.

2012-US0040984
Summary:
On an unspecified date in June of 2007, a 14 year old, 20 pound, neutered, male, Schnauzer (Miniature) canine, in fair condition, with a known medical history of kidney stones, was administered 1 tube of Advantage II Small Dog (Imidacloprid-Pyriproxyfen) once topically by the owner. On an unspecified date in December of 2007 the dog was euthanized due to kidney stones.

Assessment:
This patient was euthanized due to complications associated with a pre-existing condition.

2012-US0040985
Summary:
On 05-Sep-2012, a 2 year old, 10 pound, intact, female, Pomeranian canine, in good condition, with no known concomitant medical conditions, was administered 1 tube of Advantage II Small Dog (Imidacloprid-Pyriproxyfen) once topically by the owner. On 07-Sep-2012 the dog became ataxic, began vomiting, became inappetant, and was vocalizing. On 08-Sep-2012 the dog became lethargic. The dog presented to the veterinarian. Upon examination the dog was also tachycardic and hypothermic. The dog was given subcutaneous fluids and activated charcoal. The owner declined all other treatments and blood work. The signs continued. On 08-Sep-2012 the dog was bathed with no resolution of symptoms. On 09-Sep-2012 the dog presented again to the veterinarian having grand mal seizures. The dog was then euthanized. No necropsy was performed.

Assessment:
Death is never an expected outcome from the use of a topical product. Advantage II is a safe, non-toxic product and signs of this nature would not be anticipated. The dog presented to the veterinarian 4 days after product application having grand mal seizures. No diagnostics were performed and the dog was euthanized due to financial concerns. No necropsy was performed.

2012-US0041988

Summary:

On 16-Sep-2012, a 2 year old, 8 pound, intact female, Dachshund canine, in good condition, with a current flea infestation and mild dermatitis, was administered 1 tube of Advantage II Small Dog (Imidacloprid-Pyriproxyfen) once topically by the owner. Approximately three hours after product application the dog developed a behavioral changed and appeared agitated. She also had abnormal respiration. The dog then became ataxic began retching and was lethargic. Later in the night the dog began yelping. On the morning of 17 Sept 2012 the dog was found deceased. The results of the necropsy: 1.) Hiatal hernia with jejunal and gastric entrapment. 2.) Flea infestation with mild dermatitis.

Assessment:

A necropsy was performed and revealed the cause of death was due to a hiatal hernia with jejunal and gastric entrapment. No quality issues were noted upon product investigation.

2012-US0043058

Summary:

On approximately 21-Sep-2011, a 10 year old, 90 pound, female, Retriever Labrador (No Description) canine, in poor condition, with a concomitant medical condition of cancer, was administered 1 tube of Advantage II (unspecified) (Imidacloprid-Pyriproxyfen) once topically by the owner. On approximately 07-Sep-2012 the dog was euthanized due to the cancer. No treatments were performed.

Assessment:

The owner initially contacted Bayer Animal Health to seek advise on how to control an active flea infestation and not to report the death of this pet. Due to the long duration of the time to onset of this patient's death from when the product was used, it is very unlikely that the product has any relation to the patient's death.

2012-US0043494

Summary:

On 21-Sep-2012, a 8 year old, 60 pound, spayed female, German Shepherd Dog canine, in good condition, with a current flea infestation and bacterial otitis externa, was administered 1 tube of Advantage II Extra Large Dog (Imidacloprid-Pyriproxyfen) once topically by the owner. On 22 Sept 2012 the dog underwent a behavioral change (reclusive toward owner, digging holes in the yard and laying in them) and became anorexic. She then began vomiting and later that day passed away. The dog was not seen by a veterinarian for the clinical signs. No necropsy was performed.

Assessment:

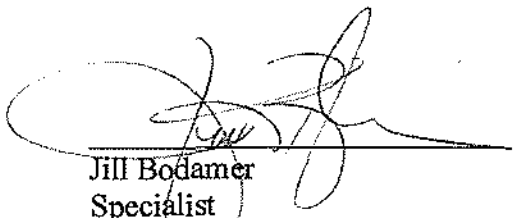
The clinical signs exhibited up to and including death are not indicative of toxicity associated with imidacloprid or pyriproxyfen. The exact cause of death could not be determined. What role, if any, the product played in this case also cannot be determined.

We believe this summary of data meets the requested information in the Agency's requirements for enhanced reporting as outlined in its January 19, 2011 communication to Bayer.

A report with the confidential sales information and additional analysis of incident rates based on doses sold is being sent to the Registration Division, Immediate Office (attn. Ms. Kimberly Nesci).

If there are any questions regarding this submission, please contact me by phone at 913.268.2082 or by e-mail at jill.bodamer@bayer.com.

Most Kind Regards,



Jill Bodamer
Specialist
Regulatory Affairs

Bayer HealthCare
Animal Health Division

August 31, 2011,

Document Processing Desk
Office of Pesticide Programs (7504P) – NonPRIA
U.S. Environmental Protection Agency
Room S-4900, One Potomac Yard
2777 South Crystal Drive
Arlington, VA 22202-4501

Attention: Ms. Venus Eagle/PM01

Subject: Advantage II Kitten (EPA Reg. No. 11556-150)
Advantage II Small Cat (EPA Reg. No. 11556-151)
Advantage II Large Cat (EPA Reg. No. 11556-152)
Advantage II Small Dog (EPA Reg. No. 11556-128)
Advantage II Medium Dog (EPA Reg. No. 11556-125)
Advantage II Large Dog (EPA Reg. No. 11556-127)
Advantage II Extra Large Dog (EPA Reg. No. 11556-130)

Please find enclosed the conditional registration requirement of enhanced quarterly incident report for Advantage II Dog and Cat registrations for the quarter starting April 1, 2011.

This submission includes the following tables covering incident reporting from April 01, 2011 through June 30, 2011:

Summary Table (multiple pages due to length)
Breed Summary
Age Range Summary
Clinical Signs Summary
Organ System Summary
Patient Weight Range Summary
Product Weight Range Summary
Route of Exposure Summary
Secondary Exposure Summary

Due to the length of some of the tables and to provide the Agency the ability to sort, this data is being provided electronically on a CD. The data was extracted from Bayer's pharmacovigilance data base (P.V. Works).

Deaths

Deaths were reported in four (4) felines that had previously received treatment with Advantage II during the period of review. Specifics are as follows:

2011-US0010189

Summary:

A 4 week old kitten of unknown weight with a heavy flea infestation and ocular discharge was nursing from a queen that was a stray with mastitis. The kitten had been administered amoxicillin, an eye ointment for ocular discharge and formula (unspecified) starting on 12April11. The queen had a partial tube of Advantage II Large Cat applied to her on 16April11 for a current flea infestation. On the morning of 17April11 the owner states the kitten appeared to take a turn for the worse. By that evening the kitten seemed cold and died in the owners arms. No necropsy examination was performed.

Assessment:

Imidacloprid, the active ingredient in Advantage is non-toxic and would not be expected to cause death or any other systemic effects. The product was applied to the queen and not to the kitten. As the kittens had a heavy flea infestation and were being treated with other medications for ocular discharge before the Advantage was used, it is unknown what part the other medications and formula played in this case. As the attending veterinarian is suspecting a metabolic disease, other etiologies must be considered in this case. It was also noted the kitten was nursing from a queen with mastitis, most likely ingesting infectious organisms during the process.

2011-US0017230

Summary:

On 12May2011 owner applied monthly dose of Advantage II Large Cat to

Slim, a 7 year old neutered male Domestic Short hair that weighs 10 pounds. 10 days later, on 22May2011 this feline collapsed. On 23May2011 the doctor examined and found this feline was very jaundiced. The cat went in to cardiac arrest and passed away while the veterinarian was obtaining blood for testing. Blood work showed what the attending veterinarian believed to be full organ function failure. Results were: Lymphocytes % low at 7.5% (12-45), Granulocyte % High at 86 (35-80), RBC High at 11.71 (4.6-10), HCT high at 50.8 % (28-49), MCH low at 12..4 pg (13-21), MCHC low at 28.7 g/dL (30-38), PLT low at 92 (100-514), ALP low <5 (10-90), ALT High 205 (20-100), TBIL High 10.8 (0.1-0.6), BUN High 82 (10-30), CA High 11.9 (8.0-11.8), PHOS High 11.2 (3.4-8.5), Glu low 57 (70-150), TP High 9.4 (5.4-8.2), and GLOB High 6.0 (1.5-5.7)
No necropsy was preformed.

Assessment:
These clinical signs are non-specific and may have multiple potential other causes. Imidacloprid and pyriproxyfen are the active ingredients of the topical acting product Advantage II Large cat. This feline present to the veterinarian 12 days after application in full organ failure. The attending veterinarian does not believe was product-related. The lot investigations showed no product quality issue evident. No necropsy was performed.

2011-US0018883
Summary:
Advantage II Small Cat was applied for the first time to a 10 year old, approximately 8.5 pound Domestic Shorthair on 29May11. The evening of 31May11, the owner came home from work to find her cat dead in the bathroom. No necropsy was performed.

Assessement:
The clinical sign reported is not consistent with a topically acting product. Death is never expected following the use of any topical product. Without a necropsy, it is impossible to determine the cause of death. QA investigation results did not reveal any product abnormalities.

Bayer HealthCare
Animal Health Division

2011-US0021320

Summary:
Owner treated a 12 year old, 4 pound, female cat with half a tube of Advantage II Large Cat and this cat immediately disappeared after application. Caller found cat dead in the back yard seven days later. No necropsy examination was performed.

Assessment:
Product was used in an off-label manner, however death after product use is not consistent with active ingredient. No necropsy was performed and it is unknown what else the cat may have been exposed to for those seven days prior to death.

We believe this summary of data meets the requested information in the Agency's requirements for enhanced reporting as outlined in its January 19, 2011 communication to Bayer.

A report with the confidential sales information and additional analysis of incident rates based on doses sold is being sent to the Registration Division, Immediate Office (attn. Ms. Kimberly Nesci).

If there are any questions regarding this submission, please contact me by phone at 913.268.2573 or by e-mail at gary.brumley@bayer.com.

Gary Brumley
Senior Consultant
Regulatory Affairs

Material Sent for Data Extraction

Reg. # 11SS6-150

Description: Amend

☑ Material(s) Sent to Data Extraction Contractors:

- ☑ New Stamped Label Dated 3/28/13
- ☐ Notification Dated _____
- ☐ New CSF(s) Dated _____
- ☐ Other: _____

☐ Decision #: _____

☐ Other Action/Comments: _____

_____

File this coversheet and attached materials in the jacket. It must be well organized and clipped together, NOT STAPLED. Then give the jacket with the coversheet and materials to staff in the Information Services Center (ISC) (Room S-4900). If a jacket is full or only available as an image, please file materials in a new jacket and bring it down to the (ISC). For further information please call 703-605-0716.

Reviewer: Jennifer Urbanski

Phone: 347-0156 Division: RD

Date: 3/28/13

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
CHEMICAL SAFETY AND
POLLUTIDN PREVENTIDN

Douglas Spilker
Bayer HealthCare LLC, Animal Health Division
PO Box 390
Shawnee Mission, KS 66201

MAR 2 8 2013

Dear Mr. Spilker:

Subject: Amendments to add new child resistant packaging
Advantage II Kitten
EPA Registration No. 11556-150
Decision Numbers: 473308
Submission Dates: December 14, 2012

The label referred to above, submitted in connection with registration under the Federal Insecticide, Fungicide, and Rodenticide Act, as amended, is acceptable. A stamped copy of the label is enclosed for your records. Please submit two copies of your final printed labeling before you release the product for shipment. If you have any questions regarding these labels, please contact Dr. Jennifer Urbanski at 703-347-0156 or urbanski.jennifer@epa.gov.

Sincerely yours,

Venus Eagle

Venus Eagle
Product Manager (01)
Insecticide-Rodenticide Branch
Registration Division (7505P)

Enclosure- Stamped Label and Science Reviews (DP408181)

Reason To Issue: New child-resistant packaging proposal. Date: 02/14/13
Supersedes: 12/12/12, 11/28/12 and 09/25/12

NOTE TO REVIEWER: [(Brackets and parentheses indicate alternate language)]

[Front Panel]

Advantage® II Kitten

Once-A-Month Topical Flea Prevention and Treatment for Cats
For Use ONLY on Cats 8 Weeks and Older and Weighing 2 – 5 lbs.

[Selected optional claims bulleted here from page 10 and/or 11]

-
-
-
-

Active Ingredients	% By Weight
Imidacloprid	9.10%
Pyriproxyfen	0.46%
Other Ingredients	90.44%
Total	100.00%

EPA Est. No. 11556-XXX-X EPA Reg No. 11556-150

KEEP OUT OF REACH OF CHILDREN

CAUTION

See back panel for Precautionary Statements.
For Directions for Use, Storage and Disposal, and First Aid see package insert inside.

ACCEPTED
MAR 2 8 2013
Under the Federal Insecticide, Fungicide, and Rodenticide Act, as amended, for the pesticide registered under:
EPA. Reg. No: 11556-150

[Back Panel]

Advantage® II Kitten

Once-A-Month Topical Flea Prevention and Treatment for Cats
For Use ONLY on Cats 8 Weeks and Older and Weighing 2 - 5 lbs.

READ THE ENTIRE LABEL BEFORE EACH USE
For the Prevention and Treatment of Flea Infestations

PRECAUTIONARY STATEMENTS

HAZARDS TO HUMANS

CAUTION: Harmful if swallowed. Causes moderate eye irritation. Avoid contact with eyes or clothing. Wash hands thoroughly with soap and warm water after handling. Keep out of reach of children. Do not contaminate feed or food.

HAZARDS TO DOMESTIC ANIMALS

For external use only. Do not apply to cats or kittens under 8 weeks of age or weighing less than 2 lbs. As with any product, consult your veterinarian before using this product on debilitated, aged, pregnant or nursing cats. Individual sensitivities, while rare, may occur after using ANY pesticide product for cats. If signs persist, or become more severe, consult a veterinarian immediately. If your cat is on medication, consult your veterinarian before using this or any other product.

Side Effects: Monitor your cat after application. Side effects, although very rare, may include signs of skin irritation such as redness, scratching, or other signs of discomfort. Gastrointestinal signs such as hypersalivation, vomiting or diarrhea have also been reported. If these or other side effects (such as lethargy) occur, consult your veterinarian or call 1-800-422-9874.

For consumer questions call 1-800-255-6826.
For medical emergencies call 1-800-422-9874.

RESTRICTIONS:

- Use only on cats or kittens 8 weeks and older. Do not apply to cats or kittens weighing less than 2 lbs. Do not use on other animals.
- Do not apply more than one (1) tube per treatment.
- Do not have contact or allow children to have contact with treated area until completely dry.

Reason To Issue:	New child-resistant packaging proposal.	Date: 02/14/13 Supersedes: 12/12/12, 11/28/12 and 09/25/12

Net Contents: [X] Tube(s), each 0.0078 fl. oz. (0.23 mL)

[Sample - Not for (Re)Sale]

Manufactured For

Bayer HealthCare LLC
Animal Health Division
P.O. BOX 390
Shawnee Mission, Kansas 66201 USA

Made in Germany

[Back Panel and/or Insert]

Advantage® II Kitten

Once-A-Month Topical Flea Prevention and Treatment for Cats
For Use ONLY on Cats 8 Weeks and Older and Weighing 2 - 5 lbs.

READ THE ENTIRE LABEL BEFORE EACH USE
For the Prevention and Treatment of Flea Infestations

DIRECTIONS FOR USE

It is a violation of Federal Law to use this product in a manner inconsistent with its labeling.

HOW TO OPEN

[OPTION 1: INSTRUCTIONS FOR BLISTER PACK]
1. Being careful not to cut close to the blister cavities, take scissors and cut off one section of the card containing a single tube.
2. Take the separated section, and cut into the blister cavity across the small side, close to the cap of the tube.
3. Peel off the foil, and take out the tube.
4. Repeat steps 1 to 3 for each tube.

[OPTION 2: INSTRUCTIONS FOR POUCH PACK]
1. Be sure tube is at bottom of pouch.
2. Using scissors, cut the pouch across the top and remove tube.

HOW TO APPLY

1. Remove one applicator tube from the package. See "HOW TO OPEN" section.

2. Hold applicator tube in an upright position facing away from you and your pet's face and eyes. Pull cap off tube.

[Visuals Depicting How to Open Applicator Tube]

3. Turn the cap around and place other end of cap back on tube.

4. Twist cap to break seal, then remove cap from tube.

5. Part the hair on the neck at the base of the skull until the skin is visible. Place the tip of the tube on the skin and squeeze the tube to expel the entire contents directly on the skin. *Do not get this product in your cat's eyes, or allow your cat to ingest this product. The product is bitter tasting and salivation may occur for a short time if the cat licks the product immediately after treatment.* Treatment at the base of the skull will minimize the opportunity for the cat to lick the product. Do not allow the product to run off.

[Visuals Depicting Application to Animal]

6. Discard empty tube as described in Storage and Disposal.

7. Under normal conditions this product is effective for a month. However, in case of severe flea infestation, retreatment may be necessary earlier than four (4) weeks. Do not retreat more often than once every fourteen (14) days. After flea control is attained, return to a monthly retreatment schedule.

PRODUCT INFORMATION

The successive feeding activity of fleas on cats frequently elicits a hypersensitivity skin disorder known as flea allergy dermatitis (FAD) or flea bite hypersensitivity. Treatment of cats with Advantage® II Kitten kills fleas and may reduce the incidence of this condition.

Advantage® II Kitten kills the existing fleas on cats within 12 hours. Reinfesting fleas are killed within 2 hours with protection against further flea infestation lasting for up to four (4) weeks. Pre-existing pupae in the environment may continue to emerge for six (6) weeks or longer depending upon the climatic conditions.

Fleas, eggs and larvae in the cat's surroundings are killed following contact with an Advantage® II Kitten treated cat. Advantage® II Kitten provides multi-stage flea control effectively breaking all flea life-cycle stages for lasting control of flea populations.

Advantage® II Kitten kills adult fleas quickly, within 12 hours, inhibits the development of immature flea life stages and prevents them from reaching the biting adult stage.

Advantage® II Kitten is waterproof and remains effective following a shampoo treatment or after exposure to rain or sunlight.

Apply monthly treatments for optimal control and prevention of fleas.

KEEP OUT OF REACH OF CHILDREN

CAUTION

PRECAUTIONARY STATEMENTS
HAZARDS TO HUMANS

CAUTION: Harmful if swallowed. Causes moderate eye irritation. Avoid contact with eyes or clothing. Wash hands thoroughly with soap and warm water after handling. Keep out of reach of children. Do not contaminate feed or food.

FIRST AID	
If Swallowed:	• Call a poison control center or doctor immediately for treatment advice. • Have person sip a glass of water if able to swallow. • Do not induce vomiting unless told to do so by the poison control center or doctor. • Do not give anything to an unconscious person.
If In Eyes:	• Hold eye open and rinse slowly and gently with water for 15-20 minutes. Remove contact lenses, if present, after the first 5 minutes, then continue rinsing eye. • Call a poison control center or doctor for treatment advice.
If On Skin	• Wash with plenty of soap and water.
HOT LINE NUMBER	
Have the product container or label with you when calling a poison control center or doctor, or going for treatment. For medical emergencies call 1-800-422-9874. For customer questions call 1-800-255-6826.	
NOTE TO PHYSICIAN	
Treat the patient symptomatically.	

HAZARDS TO DOMESTIC ANIMALS

For external use only. Do not apply to cats or kittens under 8 weeks of age or weighing less than 2 lbs. As with any product, consult your veterinarian before using this product on debilitated, aged, pregnant or nursing cats. Individual sensitivities, while rare, may occur after using ANY pesticide product for cats. If signs persist, or become more severe, consult a veterinarian immediately. If your cat is on medication, consult your veterinarian before using this or any other product.

Side Effects: Monitor your cat after application. Side effects, although very rare, may include signs of skin irritation such as redness, scratching, or other signs of discomfort. Gastrointestinal signs such as hypersalivation, vomiting or diarrhea have also been reported. If these or other side effects (such as lethargy) occur, consult your veterinarian or call 1-800-422-9874.

For consumer questions call 1-800-255-6826.
For medical emergencies call 1-800-422-9874.

RESTRICTIONS:

- Use only on cats or kittens 8 weeks and older. Do not apply to cats or kittens weighing less than 2 lbs. Do not use on other animals.
- Do not apply more than one (1) tube per treatment.
- Do not have contact or allow children to have contact with treated area until completely dry.

STORAGE AND DISPOSAL

Do not contaminate water, food or feed by storage or disposal.

Pesticide Storage: Store in a cool, dry place inaccessible to children and pets. **Pesticide Disposal and Container Handling:** Nonrefillable container. **If empty**: Do not reuse or refill this container. Place in trash or offer for recycling if available. **If partly filled**: Call your local solid waste agency or 1-800-422-9874 for disposal instructions. Never place unused product down any indoor or outdoor drain.

LIMITED WARRANTY AND LIMITATION OF DAMAGES

Bayer HealthCare LLC, Animal Health Division warrants that this material conforms to the chemical description on the label. TO THE EXTENT CONSISTENT WITH APPLICABLE LAW, BAYER MAKES NO OTHER EXPRESS OR IMPLIED WARRANTY, INCLUDING ANY OTHER EXPRESS OR IMPLIED WARRANTY OF FITNESS OR MERCHANTABILITY, and no agent of Bayer is authorized to do so except in writing with a specific reference to this warranty. Any damages arising from a breach of this warranty shall be limited to direct damages and shall not include consequential commercial damages such as loss of profits or values, etc.

For more information visit www.petparents.com

[Label on Individual Tube]

Advantage® II Kitten

9.10% Imidacloprid

0.46% Pyriproxyfen

0.0078 fl. oz. (0.23 mL)

EPA Reg. No. 11556-150

Keep Out of Reach of Children

CAUTION

Read The Entire Label Before Use

BAYER

Lot No. 0000000

[OPTION 1: Label on blister card; one card containing 1, 2, 3, 4, 5, or 6 tubes]
[OPTION 2: Label on pouch containing 1 tube]

[Additional label text for OPTION 2: THIS UNIT NOT FOR RETAIL SALE]

Advantage® II Kitten

For external use only on cats and kittens 8 weeks and older and weighing 2 -5 lbs.

9.10% Imidacloprid

0.46% Pyriproxyfen

[X] - 0.0078 fl. oz. (0.23 mL) Tube(s)

EPA Reg. No. 11556-150

BAYER

NOTE TO REVIEWER: [(Brackets and parentheses indicate alternate language)]

OPTIONAL MARKETING CLAIMS [Appearing on any panel]

- For use on cats and kittens 8 weeks of age and older
- Advantage II contains [imidacloprid], [and an/the] [insect growth regulator] [IGR] [pyriproxyfen]
- A single topical application remains effective for up to [4 weeks] [a month]
- Convenient, easy-to-apply topical solution
- Convenient, easy-to-apply and fragrance free [monthly] [topical solution]
- Once a month topical flea prevention and treatment for cats 8 weeks of age or older
- Advantage II is indicated for the prevention and treatment of fleas on cats 8 weeks of age and older
- For the prevention and treatment of flea infestations
- One treatment prevents further flea infestations for up to [4 weeks] [a month]
- Kills fleas on cats within [12] hours and continues to prevent infestations for up to [four weeks] [a month]
- Kills fleas before they lay eggs
- Larval flea stages in the cat's environment are killed following contact with an Advantage II treated cat
- Kills larval stages of fleas following contact with an Advantage II treated cat
- Kills fleas within [12] hours of application
- Stops existing flea infestations by killing adult fleas
- Prevents reinfestations by killing adult fleas before they lay eggs
- Reinfesting fleas are killed within 2 hours with protection against further flea infestation
- [Prevents] [Stops] flea eggs from hatching [into biting adults]
- Effectively breaks the flea life cycle
- [Kills] [Controls] all flea life stages
- Comprehensive flea prevention and treatment
- 3-way flea protection ([kills] [controls]) adults, larvae, and eggs
- [Prevents] [Stops] flea eggs from developing into [(biting) (adult)] fleas
- Treatment with Advantage II kills fleas and may reduce the incidence of flea allergic dermatitis [FAD] or flea bite hypersensitivity
- Flea adulticide, larvicide, and ovicide
- Kills flea eggs
- Controls flea problems
- Provides flea protection
- Controls existing fleas and flea eggs plus [and] [prevents] future flea infestations
- Advantage II may be used year-round for flea [prevention][protection]

- Contains an insect growth regulator (IGR) to kill flea eggs and prevent re-infestation
- Monthly use of Advantage II kills fleas and may prevent ([flea allergy dermatitis][flea bite hypersensitivity])
- Controls existing flea infestations on your cat and prevents further infestations
- Prevents fleas on treated cats from infesting (reinfesting)
- Remains effective after bathing
- Remains effective following shampooing
- Waterproof
- Remains effective after exposure to rain or sunlight
- Fragrance-free
- In child-resistant packaging
- Starts working through contact

Decision #: 473308
DP #: (408181)
PRIA
Parent DP #:
Submission #: 928375
E-Sub #:

DATA PACKAGE BEAN SHEET

Date: 15-Jan-2013

* * * Registration Information * * *

Registration: 11556-150 - ADVANTAGE II KITTEN

Company: 11556 - BAYER HEALTHCARE LLC

Risk Manager: RM 01 - Venus Eagle - (703) 308-8045 Room# PY1 S-7913

Risk Manager Reviewer: Jennifer Urbanski JURBANSK

Sent Date: _____ PRIA Due Date: 09-May-2013 Edited Due Date: _____

Type of Registration: Product Registration - Section 3

Action Desc: (R340) AMENDMENT;NON-FAST TRACK;REVIEW WITHIN RD, E.G. PRECAUTIONARY LAE

Ingredients: 129032, Pyriproxyfen(.46%)

129099, Imidacloprid(9.1%)

* * * Data Package Information * * *

Expedite: ◯ Yes ● No Date Sent: 10-Jan-2013 Due Back: _____

DP Ingredient: 129032, Pyriproxyfen

129099, Imidacloprid

DP Title: _____

CSF Included: ● Yes ◯ No Label Included: ● Yes ◯ No Parent DP #: _____

Assigned To		Date In	Date Out	
Organization:	RD / TRB	15-Jan-2013	3/19/13	Last Possible Science Due Date: 09-Apr-2013
Team Name:	Child Resistant Packaging	15-Jan-2013		Science Due Date:
Reviewer Name:				Sub Data Package Due Date:
Contractor Name:				

* * * Studies Sent for Review * * *

Printed on Page 2

* * * Additional Data Package for this Decision * * *

No Additional Data Packages

* * * Data Package Instructions * * *

Please review the attached data to determine if the new child resistant packaging is acceptable. Attached are the studies, the appendices, the label and the CSF. The data matrix and the cover letter are the same as for t1556-152 and can be found in that package.

Feel free to contact the company directly if need be.

Thanks!

DP#: (408181) *** Studies Sent for Review *** Decision#: (473308)

MRID	MRID Status	Citation Reference	Guideline	86-5 Status
49023801		Dixon, L. (2012) Child-Resistant Packaging (CRP) Child Panel Test of 0.23 mL Advantage II Tube in Foil Pouch 12/12/40 1or Kitten. Project Number: 12446, 200545, 152/480. Unpublished study prepared by Great Lakes Marketing Associates, Inc. 59p.		Pass (08-Jan-2013)
49023802		Dixon, L. (2012) Child-Resistant Packaging (CRP) Senior Adult Panel Test of 0.23 mL Advantage II Tube in Foil Pouch 12/12/40 for Kitten. Project Number: 38996, 12446, 200545. Unpublished study prepared by Great Lakes Marketing Associates, Inc. 239p.		Pass (08-Jan-2013)

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

CHILD-RESISTANT PACKAGING REVIEW
Technical Review Branch

IN 01/15/2013 & 03/13/2013 OUT 03/19/2013

RD, TRB, Reviewed by Rosalind L. Gross 03/19/2013

EPA Reg. No. or File Symbol 11556-125, 127, 128, 130, 150, 151 (uses11556-128 data), and 152

DP Barcode DP408182, 408183, 408184, 408185, 409881, 408181, 408179, 408177,

Decision # 473346, 473347, 473348, 473309, 473308, 473349, 473345,
EPA Petition or EUP No. _____

Date Division Received 12/19/2012

Type Product(s) Insecticide (flea product)

Data Accession No(s). MRID numbers 49023701 (GLM12443), 49023702 (GLM12443), 49022901 (GLM12442), 49022902 (GLM12442), 49023601 (GLM12445), 49023602 (GLM12445), 49022801 (GLM12441), 49022802 (GLM12441), 49022803 (GLM12447), 49022804 (GLM12447), 49060301 (GLM13047), 49060302 (GLM13047), 49060303 (GLM13049), 49060304 (GLM13049), 49023801 (GLM12446), 49023802 (GLM12446), 49023901 (GLM12444), and 49023902 (GLM12444)

Product Mgr./Chemical Review Mgr/Contact Person RM 01 Jennifer Urbanski
Division RD

Product Name(s) Advantage II Medium Dog, Advantage II Large Dog, Advantage II Small Dog, Advantage II Extra Large Dog, Advantage II Kitten, Advantage II Small Cat, and Advantage II Large Cat

Company Name(s) Bayer Healthcare LLC

Submission Purpose: Review of CRP studies to determine if they are adequate to support CRP certification for this product in 5 fill levels in a thin film pouch and 1 fill level in a thick film pouch in 2 sizes (4 or 6 pouches/ package)

Active Ingredient(s), PC code, & %: Imidacloprid 9.1%
Pyriproxyfen 0.46%

Summary of Findings

The Agency concludes all the requirements for CRP are met for EPA Registration Number 11556-125, 127, 128, 130, 150, 151, and 152 based on the more stringent definition of a senior failure in combination with the Senior Adult Use Effectiveness (SAUE) being 96% or more with the one exception noted (see conclusion for details). For the details of each study refer to the attached summary chart (selfcertreviewsummarychtbayer2013.doc).

The **CRP certifications submitted December 12, 2012** (EPA Registration Number 11556-125, 127, 128, 150, 151, and 152) and **February 14, 2013** (EPA Registration Number 11556-130) **are acceptable. The December 12, 2012** labels for EPA Registration Number 11556-125, 127, 128, 130, 150, 151, and 152 have the CRP directions used in SAUE testing. **The directions on opening the package given to consumers must be identical to those given to the seniors during testing for the pouches (see package section for exact language). Note EPA Registration Number 11556-127 (GLM12442) the fluid ounces on the label for the tube and pouch should read 0.085 fluid ounces.**

Should any human experience/epidemiological evidence indicate a problem once the product is in the marketplace, the Agency reserves the right to reexamine this data comprehensively and to question the child resistance of the package involved.

Package

The package consists of a pouch, which is the child-resistant feature, containing a white plastic tube with a white closure. The tube is opened by removing the closure, inverting it and twisting it to break the seal on the tube. Then the closure is removed and the product is dispensed. The pouch looks like:

The pouch is either a thin film PET/AL/PE 12/12/40 pouch or a thick film PET/AL/PE 23/12/50 pouch dependent on the fill size. The thin film PET/AL/PE 12/12/40 pouch is used for the 1ml, 2.5ml, 0.4ml, 0.23ml, and 0.8ml fill levels (EPA Registration Number 11556-125, 127, 128, 150, 151, and 152). The thick film PET/AL/PE 23/12/50 pouch is used for the 4ml fill level (EPA Registration Number 11556-130). The thin and thick film pouches will be in sizes of 4 or 6 pouches per package. The pouch has no instructions for opening on it. The instructions given to seniors during CRP testing were on a label given to them along with a pair of scissors. The instructions on the label said:

HOW TO OPEN

- Be sure tube is at bottom of pouch.
- Using scissors, cut the pouch across the top and remove tube.

Toxicity

The toxicity of the product, which contains 9.1% Imidacloprid and 0.46% Pyriproxyfen, is based on toxicity data for a 9.0% Imidacloprid and 0.48% Pyriproxyfen formulation. The acute oral LD_{50} study MRID 47089411 (9.0% Imidacloprid and 0.48% Pyriproxyfen) is 1098mg/kg for the female rat, no male rat was used in the study. The toxic or harmful amount for an 11.4 kg child is 12.5g (1098mg/kg x 11.4kg), which is 11.4ml of product (12.5g divided by 1.092g/ml [product density]).

Failure

For the purposes of CRP testing a child **failure** is access to 12.5g = 11.4ml or 9 pouches, whichever is less. The number of pouches is a function of the number of ml per pouch. In **no case is access to one pouch a child failure.** For the number of pouches for each product see the table below:

EPA REG #	Product Density mg/ml	Pkg Size	fill level amt ml (ml = 0.0338 fl. oz.)	fill level fl. oz.	# units = toxic amt	# units = child failure
11556-125	1092	4 or 6 pouches	1ml	0.0338 = 0.034	11.4 = 12	9
11556-127	1092	4 or 6 pouches	2.5ml	0.0845 = 0.085	4.56 = 5	5
11556-128	1092	4 or 6 pouches	0.4ml	0.01352 = 0.014	28.5 = 29	9
11556-130	1092	4 or 6 pouches	4ml	0.1352 = 0.135	2.85 = 3	3
11556-150	1092	4 or 6 pouches	0.23ml	0.007774 = 0.0078	49.56 = 50	9
11556-151 (use 11556-128)	1092	4 or 6 pouches	0.4ml	0.01352 = 0.014	28.5 = 29	9

EPA REG #	Product Density mg/ml	Pkg Size	fill level amt ml (ml = 0.0338 fl. oz.)	fill level fl. oz.	# units = toxic amt	# units = child failure
11556-152	1092	4 or 6 pouches	0.8ml	0.02704 = 0.027	14.25 = 15	9

A **pouch failure** is any opening or leakage of the pouch.
A **Senior Adult Use Effectiveness (SAUE) failure** is failure to open a pouch, tube, or pouch and tube in the 5 minute test period, or failure to open a pouch, tube, or pouch and tube in the 1 minute test period.

Analysis of Data

The CRP summaries of the test data, which agreed with the complete review for the studies, were included. A computer analysis and complete review of the 9 Child-Resistant Effectiveness (CRE) and 9 SAUE studies were not done. We used the summaries of the test data[1], a computer analysis of the worst case study and a computer analysis for the thick film pouch that underwent SAUE testing in strict accordance with 16 CFR 1700.20 were done. This means a computer analysis was done for the 4 ml thin film pouch (PET/AL/PE 12/12/40) with the lowest SAUE including the lowest CRE (MRID 49022802 (GLM12441) and 49022801 (GLM12441)) and a computer analysis was done for the 4 ml thick film pouch (PET/AL/PE 23/12/50) as a 6 pouch package (MRID 49060304 (GLM13049) and MRID 49060303 (GLM13049)). The results of our review are:

Child Study 4ml thin film pouch (PET/AL/PE 12/12/40) (lowest CRE MRID49022801 (GLM12441)) involved giving each child 4 pouches each containing 4ml of water at the start of the test. A child failure was defined as access to 3 pouches as the pouch was the child-resistant feature. The results from computer analysis were a 50 child test had 5 failures. The failures were 5 children accessing 3 pouches each. There were also 4 children who accessed 2 pouches and 11 children who accessed 1 pouch. A total 20 children accessed 1 or more pouches each. The CRP summary of the test data agreed with these results. **This study was a pass according to the child sequential test in**

1 Since the CRP summaries agreed with the complete review for the studies, they were used instead of the complete review.

16 CFR 1700.20.

Senior Adult Use Effectiveness Study 4ml thin film pouch (PET/AL/PE 12/12/40) (lowest SAUE MRID49022802 (GLM12441)) involved having the test subjects open one pouch during a 5 minute test period and one pouch during a one minute test period. Scissors were made available during testing because the test directions given to the seniors called for their use. The results from computer analysis were 95% SAUE with 5 failures to open the pouch in the 1 minute test period. **The CRP summary of the test data did not agree with these results.** The registrant defined a failure more **stringently.**[2] Based on the aforementioned more stringent definition of a failure the CRP summary results were 92% SAUE with the senior receiving one pouch for the 5 minute and 1 minute test period. The 8 failures were 5 seniors failed to open the tube during the 5 minute test period, 3 seniors failed to open the pouch and tube during the 1 minute test period. **SAUE testing was not done in strict accordance with 16 CFR 1700.20.**[3] **The study is a pass of the Senior Adult test in 16 CFR 1700.20 and the effectiveness specifications in 16 CFR 1700.15(b).**

Child Study 4ml thick film pouch (PET/AL/PE 23/12/50) as a 6 pouch package (MRID 49060303 (GLM13049)) involved giving each child 6 pouches each containing 4ml of water at the start of the test. A child failure was defined as access to 3 pouches as the pouch was the child-resistant feature. The results from computer analysis were a 50 child test had 2 failures. The failures were 2 children accessing 3 pouches each. There were also 2 children who accessed 2 pouches and 4 children who accessed 1 pouch. A total 8 children accessed 1 or more pouches each. The CRP summary of the test data agreed with these results. This **study was a pass according to the child sequential test in 16 CFR 1700.20.**

Senior Adult Use Effectiveness Study 4ml thick film pouch (PET/AL/PE 23/12/50) as a 6 pouch package (MRID 49060304 (GLM13049)) involved giving the seniors 6 pouches at the beginning of each test period and having the test subjects open one pouch during a 5 minute test period and one pouch during a one minute test period. Scissors were made available during testing because the test directions given to the seniors called for their use. The results from computer analysis were 99% SAUE with 1 failure to open the pouch in the 1 minute test period. **The CRP summary of the test data did not agree with these results.** The registrant defined a failure more **stringently.**[4] Based on the aforementioned more stringent definition of a failure the

---

2 A failure was defined as a failure to open a pouch, tube, or pouch and tube in the 5 minute test period, or failure to open a pouch, tube, or pouch and tube in the 1 minute test period.

3 The senior received one pouch not the 4 or 6 pouches in a package at the start of the 5 minute and 1 minute test period.

4 A failure was defined as a failure to open a pouch, tube, or pouch and tube in the 5

CRP summary results were 96% SAUE. The 4 failures were 1 senior failed to open the tube during the 5 minute test period, 3 seniors failed to open the pouch and tube during the 1 minute test period. **SAUE testing was done in strict accordance with 16 CFR 1700.20. The study is a pass of the Senior Adult test in 16 CFR 1700.20 and the effectiveness specifications in 16 CFR 1700.15(b).**

For the details of each study refer to the attached summary chart (selfcertreviewsummarychtbayer2013.doc).

Conclusion

Review of CRP summaries of the test data and the computer analysis of the data revealed that only 2 of the 9 SAUE studies were done in strict accordance with 16 CFR 1700.20 (EPA Registration Number 11556-130 4ml 6 pack (MRID 49060302 (GLM 13047) and MRID 49060304 (GLM13049)). However, the use of the other 7 SAUE studies where the seniors only received one pouch at the beginning of the 5 minute test period and the 1 minute test period **will be allowed based on the results for the SAUE all being 96% or above.** The **one exception is for the 4ml thin film pouch (PET/AL/PE 12/12/40), which will not be used** as either a 4 pouch or 6 pouch package per the February 14, 2013 CRP certification for EPA Registration Number 11556-130.

Furthermore, the discrepancies in the SAUE between the CRP summaries and the computer analysis were based on the registrant defining a failure more stringently than the regulations in 16 CFR 1700.20. **The Agency will accept and use the more stringent definition of a senior failure specified by the registrant (and noted herein).**

The Agency concludes all the requirements for CRP are met for EPA Registration Number 11556-125, 127, 128, 130, 150, 151, and 152 based on the more stringent definition of a senior failure in combination with the SAUE being 96% or more with the one exception noted above. For the details of each study refer to the attached summary chart (selfcertreviewsummarychtbayer2013.doc).

The **CRP certifications submitted December 12, 2012** (EPA Registration Number 11556-125, 127, 128, 150, 151, and 152) and **February 14, 2013** (EPA Registration Number 11556-130) **are acceptable. The December 12, 2012 labels** for EPA Registration Number 11556-125, 127, 128, 130, 150, 151, and 152 have the CRP directions used in SAUE testing. **The CRP directions in all locations on the final stamped label must be identical to those used in SAUE testing (see package section for exact language). Note EPA Registration Number 11556-127**

---

minute test period, or failure to open a pouch, tube, or pouch and tube in the 1 minute test period.

(GLM12442) the fluid ounces on the label for the tube and pouch should read 0.085 fluid ounces.

Should any human experience/epidemiological evidence indicate a problem once the product is in the marketplace, the Agency reserves the right to reexamine this data comprehensively and to question the child resistance of the package involved.

CRPdatasummarycht
Self Cert Summary Data **March 15, 2013**

Company Name - Bayer 11556

Chemical - Imidacloprid 9.1% & Pyriproxyfen 0.46%

Access to a toxic or harmful amt = acute oral LD_{50} 1098mg/kg female rat MRID 47089411 (July 2007) multiplied by 11.4kg = **12.5g**
Access to a toxic or harmful amt = 12.5g divided by 1.092g/ml (product density) = **11.4ml**
pouch thin = PET/AL/PE 12/12/40
pouch thick = PET/AL/PE 23/12/50
pouch is marketed as 4 pouch or 6 pouch package

A **Senior Adult Use Effectiveness failure** is failure to open: Package A pouch in the 5 minute test period, Package A tube in the 5 minute test period, Package A pouch and tube in the 5 minute test period, Package B pouch in the 1 minute test period, Package B tube in the 1 minute test period, or Package B pouch and tube in the 1 minute test period.
A **child failure** is access to 12.5g, which is equal to **11.4ml**. The number of units is a function of the number of ml per unit.
A **unit failure** is any opening or leakage of the pouch.

*** SAS value differs from GLM Summary and Report**
For child test values new corrected SAS files were submitted and reviewed.
For senior test values the discrepancy is due to more stringent definition of senior failure to include failure to access to pouch (CR feature) and/or to access tube. [Access to the tube is not part of the senior definition of failure per 16 CFR 1700.20. Resecuring for a unit package (package A or package B) is not part of the senior definition of failure per 16 CFR 1700.20.] The results are coded by GLM such that a failure to open a tube is considered a resecuring failure for the package involved. SAS interprets a failure to resecure package A (not opening the tube per GLM) as a failure to open package B. SAS interprets a failure to resecure package B (not opening the tube per GLM) as an unrecorded incident, which is why the SAS SAUE is higher than the GLM reported SAUE. For the purposes of the review of these data the GLM reported SAUE values will be used.

Self Cert Summary Data

EPA REG #	MRID	PKG Description fill size ml, size unit ml, # unit/pkg, color, (ml = 0.0338 fl. oz.)	# units = child failure	# Pkges Child Get at Begin Test	CRE # child test	SAUE % #pkg to senior	Conclusion include CRE & SAUE via computer analysis (SAS)
11556-125 GLM12443	49023701 38989 child 49023702 38990 senior	1ml thin	9	10	50 child 1 F	98 1 Pouch	**CRP Cert** date & status 12/12/2012 acceptable **Label** dated 12/12/2012 acceptable uses the same CRP directions as in SAUE study **Label is limited to SAUE test pkg instruct.** **Meet 16 CFR 1700.20 CRE Criteria - yes** **Meet 16 CFR 1700.20 SAUE Criteria - yes** The study is a pass of the child test according to the sequential test chart in 16 CFR 1700.20. The study is a pass of the senior adult test in 16 CFR 1700.20 and the effectiveness specifications in 16 CFR 1700.15(b). all requirements for CRP per 16 CFR 1700.20 - **yes**
11556-127 GLM12442	49022901 38987 child 49022902 38988 senior	2.5ml thin	5	6	50 child 0 F	100 1 Pouch	**CRP Cert** date & status 12/12/2012 acceptable **Label** dated 12/12/2012 acceptable uses the same CRP directions as in SAUE study **Label is limited to SAUE test pkg instruct.** Note fl. oz. on label for tube and pouch should read 0.085 fl. oz. **Meet 16 CFR 1700.20 CRE Criteria - yes** **Meet 16 CFR 1700.20 SAUE Criteria - yes** The study is a pass of the child test according to the sequential test chart in 16 CFR 1700.20. The study is a pass of the senior adult test in 16 CFR 1700.20 and the effectiveness specifications in 16 CFR 1700.15(b). all requirements for CRP per 16 CFR 1700.20 - **yes**

EPA REG #	MRID	PKG Description fill size ml, size unit ml, # unit/pkg, color, (ml = 0.0338 fl. oz.)	# units = child failure	# Pkges Child Get at Begin Test	CRE # child test	SAUE % #pkg to senior	Conclusion include CRE & SAUE via computer analysis (SAS)
11556-128 GLM12445	49023601 38993 child 49023602 38994 senior	0.4ml thin	9	10	50 child 0 F	98 1 Pouch	**CRP Cert** date & status 12/12/2012 acceptable **Label** dated 12/12/2012 acceptable uses the same CRP directions as in SAUE study **Label is limited to SAUE test pkg instruct.** **Meet 16 CFR 1700.20 CRE Criteria - yes** **Meet 16 CFR 1700.20 SAUE Criteria - yes** The study is a pass of the child test according to the sequential test chart in 16 CFR 1700.20. The study is a pass of the senior adult test in 16 CFR 1700.20 and the effectiveness specifications in 16 CFR 1700.15(b). all requirements for CRP per 16 CFR 1700.20 - **yes**
11556-130 GLM12441	49022801 38985 child 49022802 38986 senior	4ml thin 4 pack	3	4	50 child 5 F	92 1 Pouch 5F open pkg A tube, 3F open pkg B pouch & tube in 60 sec	**CRP Cert** date & status 2/14/2013 acceptable **Label** dated 12/12/2012 acceptable uses the same CRP directions as in SAUE study **Label is limited to SAUE test pkg instruct.** **CRE** * results from computer analysis 50 child 5 F - 5 children access 3 units, 4 children access 2 units, 11 children access 1 unit. 20 children access 1 or more units. **SAUE** * results from computer analysis 95% SAUE 5 F pkg B **Meet 16 CFR 1700.20 CRE Criteria - yes** **Meet 16 CFR 1700.20 SAUE Criteria - yes** The study is a pass of the child test according to the sequential test chart in 16 CFR 1700.20. The study is a pass of the senior adult test in 16 CFR 1700.20 and the effectiveness specifications in 16 CFR 1700.15(b). all requirements for CRP per 16 CFR 1700.20 - **yes**

EPA REG #	MRID	PKG Description fill size ml, size unit ml, # unit/pkg, color, (ml = 0.0338 fl. oz.)	# units = child failure	# Pkges Child Get at Begin Test	CRE # child test	SAUE % #pkg to senior	Conclusion include CRE & SAUE via computer analysis (SAS)
11556-130 GLM 12447	49022803 38997 child 49022804 38998 senior	4ml thick 4 pack	3	4	50 child 2 F	96 1 Pouch	**CRP Cert** date & status 2/14/2013 acceptable **Label** dated 12/12/2012 acceptable uses the same **CRP** directions as in SAUE study **Label is limited to SAUE test pkg instruct.** **CRE** * results from computer analysis 50 child 2 F - 2children access 3 units, 5 children access 1 unit. 7 children access 1 or more units. **Meet 16 CFR 1700.20 CRE Criteria -yes** **Meet 16 CFR 1700.20 SAUE Criteria -yes** The study is a pass of the child test according to the sequential test chart in 16 CFR 1700.20. The study is a pass of the senior adult test in 16 CFR 1700.20 and the effectiveness specifications in 16 CFR 1700.15(b). all requirements for CRP per 16 CFR 1700.20 - **yes**
11556-130 GLM13047	49060301 39265 child 49060302 39266 senior	4ml thin 6pack	3	6	50 child 5 F	93 6 Pouch	**CRP Cert** date & status 2/14/2013 acceptable **Label** dated 12/12/2012 acceptable uses the same CRP directions as in SAUE study **Label is limited to SAUE test pkg instruct.** **Meet 16 CFR 1700.20 CRE Criteria - yes** **Meet 16 CFR 1700.20 SAUE Criteria - yes** The study is a pass of the child test according to the sequential test chart in 16 CFR 1700.20. The study is a pass of the senior adult test in 16 CFR 1700.20 and the effectiveness specifications in 16 CFR 1700.15(b). all requirements for CRP per 16 CFR 1700.20 - **yes**

EPA REG #	MRID	PKG Description fill size ml, size unit ml, # unit/pkg, color, (ml = 0.0338 fl. oz.)	# units = child failure	# Pkges Child Get at Begin Test	CRE # child test	SAUE % #pkg to senior	Conclusion include CRE & SAUE via computer analysis (SAS)
11556-130 GLM13049	49060303 39267 child 49060304 39268 senior	4ml thick 6pack	3	6	50 child 2 F	96 6 Pouch 1F open pkg A tube, 3F open pkg B pouch & tube in 60 sec	**CRP Cert** date & status 2/14/2013 acceptable **Label** dated 12/12/2012 acceptable uses the same CRP directions as in SAUE study **Label is limited to SAUE test pkg Instruct.** **CRE** results from computer analysis 50 child 2 F - 2 children access 3 units, 2 children access 2 units, 4 children access 1 unit. 8 children access 1 or more units. **SAUE** * results from computer analysis 99% SAUE 1 F pkg B **Meet 16 CFR 1700.20 CRE Criteria - yes** **Meet 16 CFR 1700.20 SAUE Criteria - yes** The study is a pass of the child test according to the sequential test chart in 16 CFR 1700.20. The study is a pass of the senior adult test in 16 CFR 1700.20 and the effectiveness specifications in 16 CFR 1700.15(b). all requirements for CRP per 16 CFR 1700.20 - **yes**
11556-150 GLM12446	49023801 38995 child 49023802 38996 senior	0.23ml thin	9	10	50 child 0 F	96 1 Pouch	**CRP Cert** date & status 12/12/2012 acceptable **Label** dated 12/12/2012 acceptable uses the same CRP directions as in SAUE study **Label is limited to SAUE test pkg Instruct.** **Meet 16 CFR 1700.20 CRE Criteria - yes** **Meet 16 CFR 1700.20 SAUE Criteria - yes** The study is a pass of the child test according to the sequential test chart in 16 CFR 1700.20. The study is a pass of the senior adult test in 16 CFR 1700.20 and the effectiveness specifications in 16 CFR 1700.15(b). all requirements for CRP per 16 CFR 1700.20 - **yes**

EPA REG #	MRID	PKG Description fill size ml, size unit ml, # unit/pkg, color, (ml = 0.0338 fl. oz.)	# units = child failure	# Pkges Child Get at Begin Test	CRE # child test	SAUE % #pkg to senior	Conclusion Include CRE & SAUE via computer analysis (SAS)
11556-151 (use 11556-128) GLM12445	49023601 38993 child 49023602 38994 senior	0.4ml thin	9	10	50 child 0 F	98 1 Pouch	**CRP Cert** date & status 12/12/2012 acceptable **Label** dated 12/12/2012 acceptable uses the same CRP directions as in SAUE study **Label is limited to SAUE test pkg instruct.** **Meet 16 CFR 1700.20 CRE Criteria - yes** **Meet 16 CFR 1700.20 SAUE Criteria - yes** The study is a pass of the child test according to the sequential test chart in 16 CFR 1700.20. The study is a pass of the senior adult test in 16 CFR 1700.20 and the effectiveness specifications in 16 CFR 1700.15(b). all requirements for CRP per 16 CFR 1700.20 - **yes**
11556-152 GLM12444	49023901 38991 child 49023902 38992 senior	0.8ml thin	9	10	50 child 3 F	96 1 Pouch	**CRP Cert** date & status 12/12/2012 acceptable **Label** dated 12/12/2012 acceptable uses the same CRP directions as in SAUE study **Label is limited to SAUE test pkg instruct.** **Meet 16 CFR 1700.20 CRE Criteria - yes** **Meet 16 CFR 1700.20 SAUE Criteria - yes** The study is a pass of the child test according to the sequential test chart in 16 CFR 1700.20. The study is a pass of the senior adult test in 16 CFR 1700.20 and the effectiveness specifications in 16 CFR 1700.15(b). all requirements for CRP per 16 CFR 1700.20 - **yes**

Please read instructions on reverse before completing form. Form Approved, OMB No. 2070-0060

EPA

United States
Environmental Protection Agency
Washington, DC 20460

☐ **Registration**
☒ **Amendment**
☐ **Other:**

OPP Identifier Number

Application for Pesticide - Section I

1. Company/Product Number	2. EPA Product Manager	3. Proposed Classification
11556-150	V. Eagle	☒ None ☐ Restricted
4. Company/Product (Name)	PM#	
Advantage II Kitten	01	
5. Name and Address of Applicant *(Include ZIP Code)*	6. **Expedited Review.** In accordance with FIFRA Section 3(c)(3)(b)(I), my product is similar or identical in composition and labeling to:	
Bayer HealthCare LLC, Animal Health Division PO Box 390 Shawnee Mission, KS 66201	EPA Reg. No. _____	
☐ *Check if this is a new address*	Product Name _____	

Section - II

☒ Amendment – Explain below.
☐ Resubmission in response to Agency letter dated _____
☐ Notification - Explain below.
☐ Final printed labels in response to Agency letter dated _____
☐ "Me Too" Application
☐ Other - Explain below

Explanation: [R340] - Amendment requiring data review within RD (new Child-Resistant Packaging) with respective changes in package opening instructions. See attachment for details.

Section - III

1. Material This Product Will Be Packaged In:

Child-Resistant Packaging	Unit Packaging	Water Soluble Packaging	2. Type of Container
☒ Yes*	☐ Yes	☐ Yes	☐ Metal
☐ No	☒ No	☒ No	☒ Plastic Tube
	If "Yes" Unit Packaging wgt. / No. per container	If "Yes" Package wgt. / No. per container	☐ Glass
***Certification must be submitted**			☒ Paper
			☒ Other (Specify) Foil

3. Location of Net Contents Information	4. Size(s) Retail Container	5. Location of Label Directions
☒ Label ☐ Container	0.23 mL tube/4 or 6 per box	☐ On Label ☒ On labeling accompanying product

6. Manner in Which Label is Affixed to Product ☒ Lithograph ☐ Paper glued ☐ Stenciled ☐ Other _____

Section - IV

1. Contact Point *(Complete items directly below for identification of individual to be contacted, if necessary, to process this application)*

Name	Title	Telephone No. (Include Area Code)
Douglas A. Spilker, Ph.D.	Manager, EPA Reg. Affairs	913-268-2751

Certification

I certify that the statements I have made on this form and all attachments thereto are true, accurate and complete. I acknowledge that any knowingly false or misleading statement may be punishable by fine or imprisonment or both under applicable law.

6. Date Application Received (Stamped)

2. Signature	3. Title
Douglas A. Spilker	Manager, EPA Reg. Affairs
4. Typed Name	5. Date
Douglas A. Spilker (doug.spilker@bayer.com)	14 Dec 2012

EPA Form 8570-1 (Rev. 8-94) Previous editions are obsolete — White- EPA File Copy (original) Yellow- Applicant Copy

Form Approved OMB Nos. 2070-0060; 2070-0057; 2070-0107; 2070-0122; 2070-0164

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
1200 Pennsylvania Avenue, N.W.
WASHINGTON, D.C. 20460

Paperwork Reduction Act Notice: The public reporting burden for this collection of information is estimated to average 1.25 hours per response for registration and 0.25 hours per response for reregistration and special review activities, including time for reading the instructions and completing the necessary forms. Send comments regarding burden estimate or any other aspect of this collection of information, including suggestions for reducing the burden to: Director, Collection Strategies Division (2822T), U.S. Environmental Protection Agency, 1200 Pennsylvania Avenue, N.W., Washington, DC 20460. Do not send the completed form to this address.

Certification with Respect to Citation of Data

Applicant's/Registrant's Name, Address, and Telephone Number	EPA Registration Number/File Symbol
Bayer HealthCare LLC, Animal Health Div., POB 390, Shawnee Mission KS 66201 (913-268-2751)	11556-150
Active Ingredient(s) and/or representative test compound(s) Imidacloprid + Pyriproxyfen	Date December 14, 2012
General Use Pattern(s) (list all those claimed for this product using 40 CFR Part 158) Indoor; Non-food Use	Product Name Advantage II Kitten

NOTE: If your product is a 100% repackaging of another purchased EPA-registered product labeled for all the same uses on your label, you do not need to submit this form. You must submit the Formulator's Exemption Statement (EPA Form 8570-27).

☐ I am responding to a Data-Call-In Notice, and have included with this form a list of companies sent offers of compensation (the Data Matrix form should be used for this purpose).

SECTION I: METHOD OF DATA SUPPORT (Check one method only)

☐ I am using the cite-all method of support, and have included with this form a list of companies sent offers of compensation (the Data Matrix form should be used for this purpose).	☑ I am using the selective method of support (or cite-all option under the selective method), and have included with this form a completed list of data requirements (the Data Matrix form must be used).

SECTION II: GENERAL OFFER TO PAY

[Required if using the cite-all method or when using the cite-all option under the selective method to satisfy one or more data requirements]

☑ I hereby offer and agree to pay compensation, to other persons, with regard to the approval of this application, to the extent required by FIFRA.

SECTION III: CERTIFICATION

I certify that this application for registration, this form for reregistration, or this Data-Call-In response is supported by all data submitted or cited in the application for registration, the form for reregistration, or the Data-Call-In response. In addition, if the cite-all option or cite-all option under the selective method is indicated in Section I, this application is supported by all data in the Agency's files that (1) concern the properties or effects of this product or an identical or substantially similar product, or one or more of the ingredients in this product; and (2) is a type of data that would be required to be submitted under the data requirements in effect on the date of approval of this application if the application sought the initial registration of a product of identical or similar composition and uses.

I certify that for each exclusive use study cited in support of this registration or reregistration, that I am the original data submitter or that I have obtained the written permission of the original data submitter to cite that study.

I certify that for each study cited in support of this registration or reregistration that is not an exclusive use study, either: (a) I am the original data submitter; (b) I have obtained the permission of the original data submitter to use the study in support of this application; (c) all periods of eligibility for compensation have expired for the study; (d) the study is in the public literature; or (e) I have notified in writing the company that submitted the study and have offered (i) to pay compensation to the extent required by sections 3(c)(1)(F) and/or 3(c)(2)(B) of FIFRA; and (ii) to commence negotiations to determine the amount and terms of compensation, if any, to be paid for the use of the study.

I certify that in all instances where an offer of compensation is required, copies of all offers to pay compensation and evidence of their delivery in accordance with sections 3(c)(1)(F) and/or 3(c)(2)(B) of FIFRA are available and will be submitted to the Agency upon request. Should I fail to produce such evidence to the Agency upon request, I understand that the Agency may initiate action to deny, cancel or suspend the registration of my product in conformity with FIFRA.

I certify that the statements I have made on this form and all attachments to it are true, accurate, and complete. I acknowledge that any knowingly false or misleading statement may be punishable by fine or imprisonment or both under applicable law.

Signature	Date	Typed or Printed Name and Title
[signature]	3-28-13	Douglas A. Spilker, Manager- EPA Reg. Affairs

EPA Form 8570-34 (12-2003) Electronic and Paper versions available. Submit only Paper version.

Bayer HealthCare
Animal Health

Via Federal Express

December 14, 2012

Document Processing Desk (REGFEE)
Office of Pesticide Programs (7504P)
U.S. Environmental Protection Agency
Room S-4900, One Potomac Yard
2777 South Crystal Drive
Arlington, VA 22202-4501

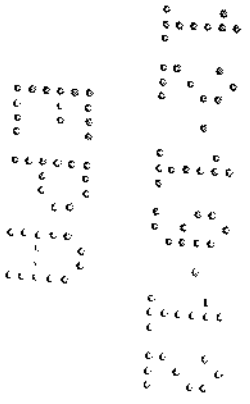
Bayer HealthCare LLC
Animal Health
P.O. Box 390
Shawnee Mission, KS 66201-0390

Attention: Ms. Venus Eagle
Registration Division

Subject: Applications for Amendment of the Registrations of:
Advantage II Kitten (EPA Reg No. 11556-150)
Advantage II Small Cat (EPA Reg. No. 11556-151)
Advantage II Large Cat (EPA Reg. No. 11556-152)
New Child-resistant packaging review (R340)

Dear Ms. Eagle:

Enclosed with this cover letter are applications for amendment of the registration of the subject three (3) companion animal (cat) spot-on products, as well as all the appropriate supporting documents and data. The purpose of this cover letter is to provide an explanatory overview of the submission which may aid in the processing of the enclosed information and respective registration applications.



Purpose of Registration Action: Bayer HealthCare, Animal Health Division, is proposing to use new child-resistant packaging for the three *Advantage II* cat products. Associated with the new CRP, new opening instructions have been added to the enclosed proposed draft labeling, text dated 12/12/12. The appropriate child resistant packaging studies are enclosed for Agency review.

Child Resistant Packaging Testing: As the Agency's files will show, because the acute oral toxicity value for the product formulation is below the 1500 mg/kg "trigger," and because this is a residential use, the products must be marketed in Child-Resistant Packaging (CRP). We currently have acceptable CRP packaging (designated as OPTION 1) data on file with the Agency (and the respective CRP Certification letters), but it is our desire to replace the current packaging with a different CRP packaging material (designated as OPTION 2). To do so, we also needed to revise the opening instructions. These new opening instructions were used in the enclosed CRP testing studies.

With regard to the overall CRP testing of the various packaging configurations, Bayer is aware of PR Notice 97-9 regarding the electronic submission of CRP test data, and therefore these data have been prepared appropriately and are included on CDs. CRP certification letters are also enclosed.

Packaging: Based on earlier CRP testing, the individual tubes alone did not qualify as child-resistant, and therefore were sold in child-resistant blisters. The current packaging for the products (designated as OPTION 1) has an outer cardboard carton with the tubes in a child-resistant blister. Instead of marketing the tubes in a blister pack, Bayer Animal Health would like the option (designated as OPTION 2) to market the product in a sealed "treasure chest" outer box containing a certain number (4 or 6) of single pouches (a single tube enclosed in a child-resistant pouch). The single pouches are made from aluminum foil [material# 01446067; PET/AL/PE 12/12/40] for the existing tubes.

The single-tube pouches will be packaged in one of two sizes of "treasure chest" outer boxes (4-tube pack/box dimension 108 x 34 x 120 mm or 6-tube pack/ box dimension 108 x 34 168 mm). However, the component of the single pouches, the aluminum pouch (and not the tube or box), is designed to be child resistant. **Please note that there are no studies submitted for the Advantage II Small Cat (11556-151) product,** since **the tube size (0.4 ml) is identical to that of the Advantage II Small Dog product (11556-128); the respective studies to support this tube size are being submitted concurrently with this application with the dog submission.**

Label Modifications: The enclosed draft labeling, date of draft 12/12/12, has been revised from previous draft labeling versions to add the new opening instructions (OPTION 2) – see especially highlighted draft label. See Amendment attachments for detailed information. No additional data are enclosed beyond those required for CRP certification.

We would also like to bring to your attention that concurrently with this submission, there is a submission for use of the new CRP with the four *Advantage II* dog products (11556-125, -127, -128, -130). We hope this overview cover letter is helpful in processing the attached applications. If you have any questions, please do not hesitate to call me at (913) 268-2751.

Sincerely,

Douglas A. Spilker. Ph. D.
Manager, EPA Regulatory Affairs
Doug.Spilker@Bayer.com

Enclosures

Document Processing Desk (REGFEE)
Office of Pesticide Programs (7504P)
U.S. Environmental Protection Agency
Room S-4900, One Potomac Yard
2777 South Crystal Drive
Arlington, VA 22202-4501

Enclosures:

Advantage II Kitten (11556-150)

- 1 copy proof of PRIA payment
- 1 copy Advantage II Kitten Application for Pesticide Registration with Application Attachment and two Appendices:
  Appendix 1 – CRP Data Review for Certification (Child Panel) – ID 38995
  Appendix 2 – CRP Data Review for Certification (Adult Panel) – ID 38996
- 3 copies draft labels, date of draft 12/12/12
- 1 copy draft label, date of draft 12/12/12 (highlighted)
- 1 copy CRP Certification letter
- 1 copy data matrix (confidential)
- 1 copy public data matrix
- Form 8570-34
- 1 copy data transmittal document
- 3 copies Bayer Report ID 38995
- 3 copies Bayer Report ID 38996
-

Advantage II Small Cat (11556-151)

- 1 copy proof of PRIA payment
- 1 copy Advantage II Small Cat Application for Pesticide Registration with Application Attachment
- 3 copies draft labels, date of draft 12/12/12
- 1 copy draft label, date of draft 12/12/12 (highlighted)
- 1 copy CRP Certification letter
- 1 copy data matrix (confidential)
- 1 copy public data matrix
- Form 8570-34

Advantage II Large Cat (11556-152)

- 1 copy proof of PRIA payment
- 1 copy Advantage II Large Cat Dog Application for Pesticide Registration with Application Attachment and two Appendices:
  Appendix 1 – CRP Data Review for Certification (Child Panel) – ID 38991
  Appendix 2 – CRP Data Review for Certification (Adult Panel) – ID 38992
- 3 copies draft labels, date of draft 12/12/12
- 1 copy draft label, date of draft 12/12/12 (highlighted)
- I copy CRP Certification letter
- I copy data matrix (confidential)
- 1 copy public data matrix
- Form 8570-34
- 1 copy data transmittal document
- 3 copies Bayer Report ID 38991
- 3 copies Bayer Report ID 38992

ATTACHMENT FOR
APPLICATION FOR PESTICIDE REGISTRATION
December 14, 2012

Advantage II Kitten (EPA Reg. No. 11556-150)

Purpose of Registration Action: Please find enclosed for the Agency's review and acceptance revised draft labeling, dated 12/12/12, for the subject product. The revisions to this label are only reflective of our enclosed proposal for an additional new child-resistant packaging. There have been no revisions of any efficacy claims. Please see the highlighted version of the draft label that shows the changes.

We currently have acceptable CRP packaging (designated as OPTION 1) data on file with the Agency (and the respective CRP Certification letters), but it is our desire to replace the current packaging with a different CRP packaging material (designated as OPTION 2). To do so, we also needed to revise the opening instructions. These new opening instructions were used in the enclosed Child-resistant packaging testing studies.

Packaging: Based on earlier CRP testing, the individual tubes alone did not qualify as child-resistant, and therefore were sold in child-resistant blisters. The current packaging for the products (designated as OPTION 1) has an outer cardboard carton with the tubes in a child-resistant blister. Instead of marketing the tubes in a blister pack, Bayer Animal Health would like the option (designated as OPTION 2) to market the product in a sealed "treasure chest" outer box containing a certain number (4 or 6) of single pouches (a single tube enclosed in a child-resistant pouch). The single pouches are made of aluminum foil [material# 01446067; PET/AL/PE 12/12/40] for the existing tubes.

The single-tube pouches will be packaged in one of two sizes of "treasure chest" outer boxes (4-tube pack/box dimension 108 x 34 x 120 mm or 6 tube pack/ box dimension 108 x 34 168 mm). However, the component of the single pouches, the aluminum pouch (and not the tube or box), is designed to be child resistant.

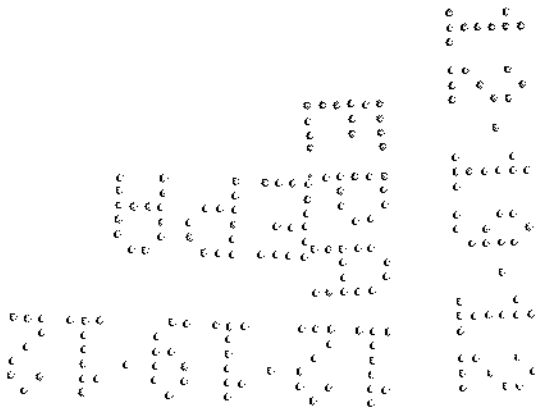
Labeling Changes: The only proposed change to the draft labeling is:

Page 4: Addition of new opening instructions (OPTION 2) – see especially

highlighted draft label.

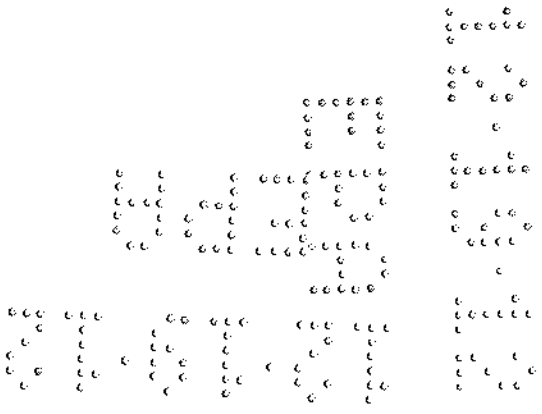
No other substantive changes have been made to this label, except for those listed above. Therefore, as soon as the data are reviewed and found acceptable, we hope that these changes to the label can be accepted by the Agency for this product, as well as, for the revised labels of the other Advantage II cat products – Advantage II Small Cat & Advantage II Large Cat - submitted concurrently with this application.

If there are any questions regarding these revisions, please contact us immediately [doug.spilker@bayer.com ; (913)-268-2751].



Appendix 1

CRP Data Review for Certification (Child Panel) – ID 38995



GREAT LAKES MARKETING RESEARCH
3361 EXECUTIVE PARKWAY, SUITE 201 | TOLEDO, OH 43606
TEL 419.534.4700 | FAX 419.531.8950 | WWW.GLM.COM

Child Panel

CRP Data Review for Certification

Date: December 4, 2012
Package: 0.23mL Advantage® II Tube in Foil Pouch 12/12/40 for Kitten
GLM: 12446 (ID# 38995)

Failure level	Each child was given ten pouches containing tubes. The tubes are not child-resistant. Access to nine was considered a failure. Any opening or leakage was considered a failure.
Child received	At the beginning of each test period, the child received ten pouches. The pouches contained water filled tubes. The tubes were not child-resistant.
Age distribution for children	50 children Age 42-44 months 30% (8 males, 7 females) Age 45-48 months 40% (10 males 10 females) Age 49-51 months 30% (7 males, 8 females)
Access rate	0 children accessed nine pouches in the first five minutes 0 children accessed nine pouches in the second five minutes 0 children accessed in the full ten-minute test period A total of 50 children were tested, First five minutes: 100% Child Effectiveness Full ten minutes: 100% Child Effectiveness
Sites	A total of 16 sites were used to complete the testing of the children. A complete list of site information is detailed in the report. Site 0123: 2 children, Site 0195: 2 children, Site 0218: 2 children, Site 0231: 2 children, Site 0294: 4 children, Site 0757: 2 children, Site 0759: 4 children, Site 1002: 2 children, Site 1032: 2 children, Site 1344: 2 children, Site 3330: 2 children, Site 3351: 6 children, Site: 3476: 2 children, Site 7170: 4 children, Site 7252: 8 children, Site 7303: 4 children
Testers	A total of 7 testers were used to complete the panel. Tester 31: 14 children, Tester 74: 12 children, Tester 21: 6 children, Tester 64: 6 children, Tester 83: 6 children, Tester 75: 4 children, Tester 35: 2 children
Findings	**This analysis shows that the package described herein meets the requirements of 40 CFR Part 157.**
Data collected and verified by:	Great Lakes Marketing 3361 Executive Parkway Toledo, Ohio 43606 Lori Mitchell Dixon, PhD, Project Director

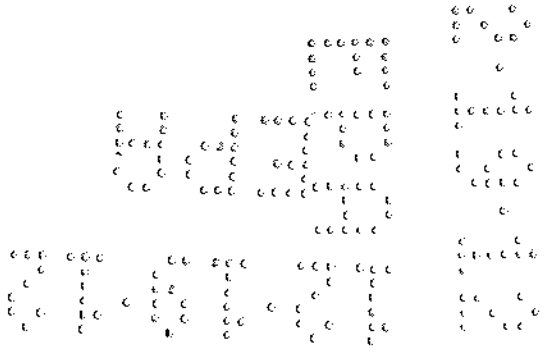
Child-Resistant Packaging (CRP) Child Panel Test of 0.23mL Advantage® II Tube in Foil Pouch 12/12/40 for Kitten

1. Introduction and Purpose

Bayer Animal Health, Shawnee, Kansas, has been marketing Advantage® II containing 9.1% imidacloprid and 0.46% pyriproxyfen as a spot-on formulation for dogs and cats for the control of fleas (all stages) for several years. This product is sold in four different volumes for dogs and three different volumes for cats. The volumes are based on body weight bands. Canine dosages are 0.4-mL (for dogs up to and including 10 lbs body weight), 1.0mL (for dogs between 11 and 20 lbs), 2.5mL (for dogs between 20 and 55 lbs) and 4.0mL (for dogs greater than 55 lbs). Dose amounts (mL) are filled in individual tubes and each dose size (mL) is currently available in two different package quantities – a 4-tube blister package and a 6-tube blister package. Feline dosages are 0.23mL (for cats and kittens 8 weeks and older and under 5 lbs), 0.4mL (for cats and kittens 8 weeks and older and 5 to 9 lbs) and 0.8mL (for cats 8 weeks and older and 9 lbs and over). As with the canine presentations, the dose amounts (mL) are filled in individual tubes and each dose size (mL) is available in two different package quantities- a 4-tube blister package and a 6-tube blister package.

Instead of marketing the tubes in a blister package, Bayer Animal Health now wants to market the product in a "treasure chest" outer box containing a certain number (4 or 6) of single pouches (a single tube enclosed in a child-resistant pouch). The single pouches are made from aluminum foil (material# 01446067; PET/AL/PE 12/12/40 and/or (material# 80685238 PET/AL/PE 23/12/50) for all sizes (volumes) of the existing tubes based on the results of the child-resistant package (CRP) testing. The selected single pouches will be packaged in one of two sizes of " treasure chest boxes" (4-tubes pack/ box dimension 108 x 34 x 120 mm & 6-tubes pack/ box dimension 108 x 34 x 168 mm).

As the acute toxicity for the Advantage® II formulation in a laboratory animal study with adult rats was below the 1500 mg/kg criteria of 40 CFR Part 157.22(a)(1) and as the product will be recommended for residential use, the product must be packaged in a child-resistant packaging. Based on an earlier CRP testing, the individual tubes alone did not qualify as child-resistant, and therefore were sold in child-resistant blister packages. Thus, the component of the single pouches, the aluminum pouch (and not the enclosed tube), is designed to be child resistant. After discussions with Dr. Rosalind Gross of EPA for the development of the original CRP blister packaging, Bayer Animal Health had agreed to the following criteria for child-resistant packaging testing.



Calculation of the Toxic Dose to a Child

The acute oral LD_{50} for Advantage® II product (formulation with 9.0% imidacloprid and 0.48%pyriproxyfen) was determined to be 1,098 mg/kg for female rats.[1]

The number of different sized (volume) tubes that would have to be ingested to induce toxicity in a 25 lb (11.4 kg) child is summarized in Table 1. "Toxic dose" for this product as defined in 40 CFR Part 157.22 and that confirmed by Dr. Rosalind Gross of US EPA is the acute oral LD_{50} value. The density of the product, 1.092 g/mL, was used in the supporting calculations. Therefore, the toxic dose for a 25 lb (11.4 kg) child amounts to 11.5 mL of Advantage® II formulation.

Table 1.
Tube Sizes, Number of Tubes as Toxic Dose for a Child, and Test Failure Criteria

Advantage® II Tube Size (mL)	No. of Tubes* Constitute as Toxic Amount for a Child	Test Failure Criteria (F) (# Tubes Accessed by a Child)
0.23	**50 (49.9)**	**9****
0.4	29 (28.7)	9
0.8	15 (14.4)	9
1.0	12 (11.5)	9
2.5	5 (4.6)	5
4.0	3 (2.9)	3

*Number in the parenthesis is rounded off to the next higher integer. All tubes are single use only, which means each tube contents are used as a single application.
**Per EPA guidance, accessing a minimum of 9 tubes are recommended as the test failure criteria for child panel testing when 9 tubes represent a toxic dose for a child.

Child-Resistant Package (CRP) Testing of Single Pouches

Bayer's Advantage® II single pouches will be made from two different aluminum (AL) foil types. Each aluminum foil contains a layer of polyethylene terephthalate (PET) on the outside and a layer of polyethylene (PE) on the inside. The specifications for the two foil types are as follows: 1) PET/AL/PE; 12/12/40 microns (material# 01446067) and 2) PET/AL/PE; 23/12/50 microns (material# 80685238).

[1] MRID No. 47089411, "An acute oral LD_{50} study in the rat with M880 Insecticide," EPA Guideline No. 870.1100, Bayer Report No. 75922 (ID No. 23792), D.A. Eigenberg, 2007, 34 pp.

Bayer has conducted CRP testing of single pouches each one containing a 4.0mL, 2.5mL, 1mL, 0.8mL, 0.4mL or 0.23mL tube. The first 4 sizes will continue to be marketed for use in dogs and the last three sizes will continue to be marketed for use in cats. Please note, 0.4mL size is common for both dogs and cats. Therefore, the CRP testing of single pouches made from 12/12/40 aluminum foil type or 23/12/50 aluminum foil type for all sizes of the product would include for each foil type 6 CRP studies (i.e., 6 child panels + 6 senior adult panels) for the dogs and cats. As a guideline requirement for the CRP testing, all plastic tubes were filled with appropriate fill volume of pure water.

The pouch specifications, identification details, and photographs for the pouch tested are presented in Appendix 3.

Child-Resistant Packaging (CRP) Child Panel Test of 0.23mL Advantage® II Tube in Foil Pouch 12/12/40

Great Lakes Marketing Research (GLM) conducted a child panel test of 0.23mL Advantage® II Tube in Foil Pouch 12/12/40, Batch No. KP07V7B, using a panel of 50 children aged 42-51 months. The test protocol prescribed in the Federal Register, Title 16, Part 1700.20 was followed.

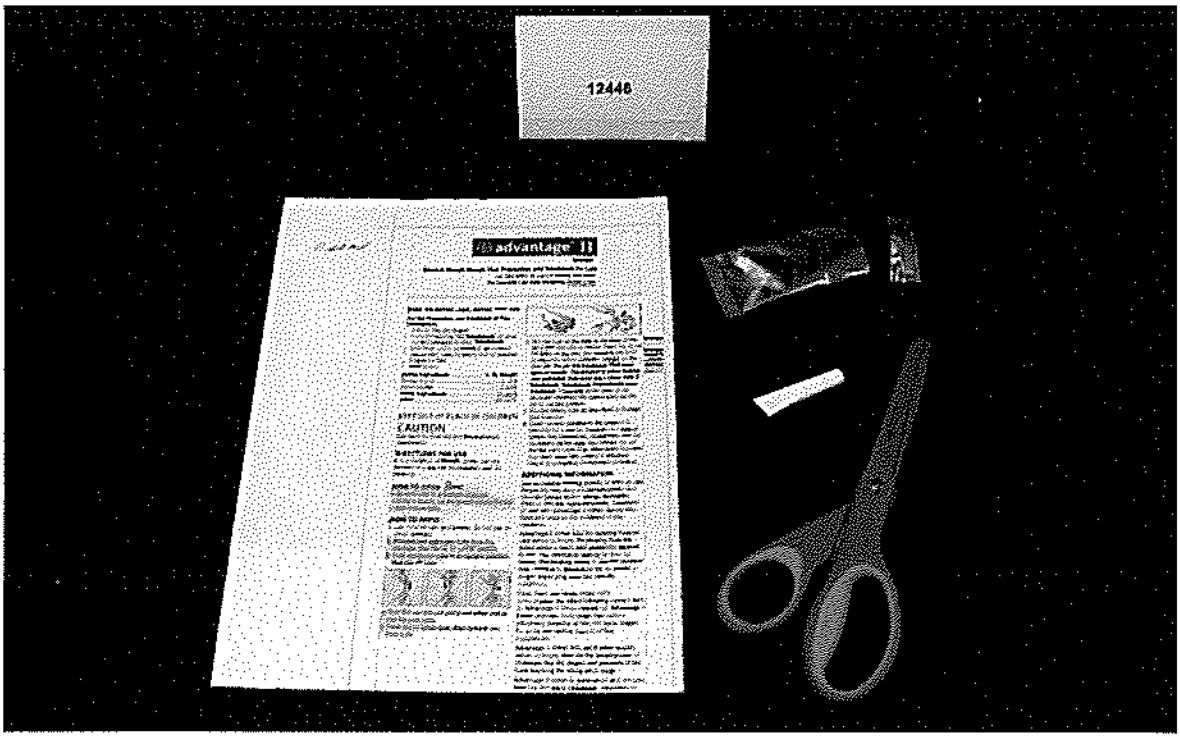
Photographs

Ten pouches (12/12/40), each containing a 0.23mL tube, as given to a child for testing (GLM Project No. 12446).

Photographs

Ten pouches (12/12/40), each containing a 0.23mL tube, as given to a child for testing. One pouch shows its reverse side (GLM Project No. 12446).

Photographs



Scissors were used for a demonstration by the tester only. A pouch (12/12/40) is photographed showing one end of the pouch cut off with the scissors and the 0.23mL tube is removed from the pouch (GLM Project No. 12446).

Appendix 2

CRP Data Review for Certification (Adult Panel) – ID 38996

GREAT LAKES MARKETING RESEARCH

3361 EXECUTIVE PARKWAY, SUITE 201 | TOLEDO, OH 43606
TEL 419.534.4700 | FAX 419.531.8950 | WWW.GLM.COM

Senior Panel

CRP Data Review for Certification

Date: December 05, 2012
Package: 0.23mL Advantage® II Tube in Pouch Foil 12/12/40 for Kitten
GLM: 12446 (ID # 38996)

Failure level	Failures include those who were unable to open the first pouch and tube, or the second pouch and tube, or unable to open the second pouch and tube in the required 60 seconds.
Adult received	At the beginning of each test period, the adult received one pouch. The adult was allowed up to five-minutes to familiarize themselves with opening the pouch and the tube. The second pouch the adult received required them to open both the pouch and the tube within the one-minute test period.
Age distribution for adults	100 adults Age 50-54 years 25% (8 males, 17 females) Age 55-59 years 25% (7 males, 18 females) Age 60-70 years 50% (15 males, 35 females)
Access rate	0 adults failed to open package A pouch 3 adults failed to open package A tube 0 adults failed to open package B pouch 0 adults failed to open package B tube 1 adult failed to open package B pouch and tube in the required 60 seconds 4 total failures **96.0%** Senior Adult Use Effectiveness
Sites	A total of 9 senior adult test sites were used. Site 090: 24 adults, Site 158: 17 adults, Site 85: 14 adults, Site 107: 12 adults, Site 072: 12 adults, Site 143: 9 adults, Site 003: 7 adults, Site 243: 4 adults, Site 047: 1 adult
Testers	A total of 5 testers were used. Tester 85: 32 adults, Tester 71: 31 adults, Tester 30: 22 adults, Tester 40: 10 adults, Tester 88: 5 adults
Findings	**This analysis shows that the package described herein meets the requirements of 40 CFR Part 157.**
Data collected and verified by:	Great Lakes Marketing Research 3361 Executive Parkway Toledo, Ohio 43606 Lori Mitchell Dixon, PhD, Project Director

Package Description: 0.23mL Advantage® II
Tube in Pouch Foil 12/12/40

Child-Resistant Packaging (CRP) Senior Adult Panel Test of 0.23mL Advantage® II Tube in Pouch Foil 12/12/40 for Kitten

1. Introduction and Purpose

Bayer Animal Health, Shawnee, Kansas, has been marketing Advantage® II containing 9.1% imidacloprid and 0.46% pyriproxyfen as a spot-on formulation for dogs and cats for the control of fleas (all stages) for several years. This product is sold in four different volumes for dogs and three different volumes for cats. The volumes are based on body weight bands. Canine dosages are 0.4-mL (for dogs up to and including 10 lbs body weight), 1.0-mL (for dogs between 11 and 20 lbs), 2.5-mL (for dogs between 20 and 55 lbs) and 4.0-mL (for dogs greater than 55 lbs). Dose amounts (mL) are filled in individual tubes and each dose size (mL) is currently available in two different package quantities – a 4-tube blister package and a 6-tube blister package. Feline dosages are 0.23-mL (for cats and kittens 8 weeks and older and under 5 lbs), 0.4-mL (for cats and kittens 8 weeks and older and 5 to 9 lbs) and 0.8-mL (for cats 8 weeks and older and 9 lbs and over). As with the canine presentations, the dose amounts (mL) are filled in individual tubes and each dose size (mL) is available in two different package quantities- a 4-tube blister package and a 6-tube blister package.

Instead of marketing the tubes in a blister package, Bayer Animal Health now wants to market the product in a "treasure chest" outer box containing a certain number (4 or 6) of single pouches (a single tube enclosed in a child-resistant pouch). The single pouches are made from aluminum foil (material# 01446067; PET/AL/PE 12/12/40 and/or (material# 80685238 PET/AL/PE 23/12/50) for all sizes (volumes) of the existing tubes based on the results of the child-resistant package (CRP) testing. The selected single pouches will be packaged in one of two sizes of " treasure chest boxes" (4-tubes pack/ box dimension 108 x 34 x 120 mm & 6-tubes pack/ box dimension 108 x 34 x 168 mm).

As the acute toxicity for the Advantage® II formulation in a laboratory animal study with adult rats was below the 1500 mg/kg criteria of 40 CFR Part 157.22(a)(1) and as the product will be recommended for residential use, the product must be packaged in a child-resistant packaging. Based on an earlier CRP testing, the individual tubes alone did not qualify as child-resistant, and therefore were sold in child-resistant blister packages. Thus, the component of the single pouches, the aluminum pouch (and not the enclosed tube), is designed to be child resistant. After discussions with Dr. Rosalind Gross of EPA for the development of the original CRP blister packaging, Bayer Animal Health had agreed to the following criteria for child-resistant packaging testing.

Calculation of the Toxic Dose to a Child

The acute oral LD_{50} for Advantage® II product (formulation with 9.0% imidacloprid and 0.48%pyriproxyfen) was determined to be 1,098 mg/kg for female rats.[1]

The number of different sized (volume) tubes that would have to be ingested to induce toxicity in a 25 lb (11.4 kg) child is summarized in Table 1."Toxic dose" for this product as defined in 40 CFR Part 157.22 and that confirmed by Dr. Rosalind Gross of US EPA is the acute oral LD_{50} value. The density of the product, 1.092 g/mL, was used in the supporting calculations. Therefore, the toxic dose for a 25 lb (11.4kg) child amounts to 11.5mL of Advantage® II formulation.

Table 1

Tube Sizes, Number of Tubes as Toxic Dose for a Child, and Test Failure Criteria

Advantage® II Tube Size (mL)	No. of Tubes* Constitute as Toxic Amount for a Child	Test Failure Criteria (F) (# Tubes Accessed by a Child)
0.23	**50 (49.9)**	**9****
0.4	29 (28.7)	9
0.8	15 (14.4)	9
1.0	12 (11.5)	9
2.5	5 (4.6)	5
4.0	**3** (2.9)	3

*Number in the parenthesis is rounded off to the next higher integer. All tubes are single use only, which means each tube contents are used as a single application.

**Per EPA guidance, accessing a minimum of 9 tubes are recommended as the test failure criteria for child panel testing when 9 tubes represent a toxic dose for a child.

Child-Resistant Package (CRP) Testing of Single Pouches

Bayer's Advantage® II single pouches will be made from two different aluminum (AL) foil types. Each aluminum foil contains a layer of polyethylene terephthalate (PET) on the outside and a layer of polyethylene (PE) on the inside. The specifications for the two foil types are as follows: 1) PET/AL/PE; 12/12/40 microns (material# 01446067) and 2) PET/AL/PE; 23/12/50 microns (material# 80685238).

[1] MRID No. 47089411, "An *acute oral LD_{50} study in the rat with M880 Insecticide,*" EPA Guideline No. 870.1100, Bayer Report No. 75922 (ID No. 23792), D.A. Eigenberg, 2007, 34 pp.

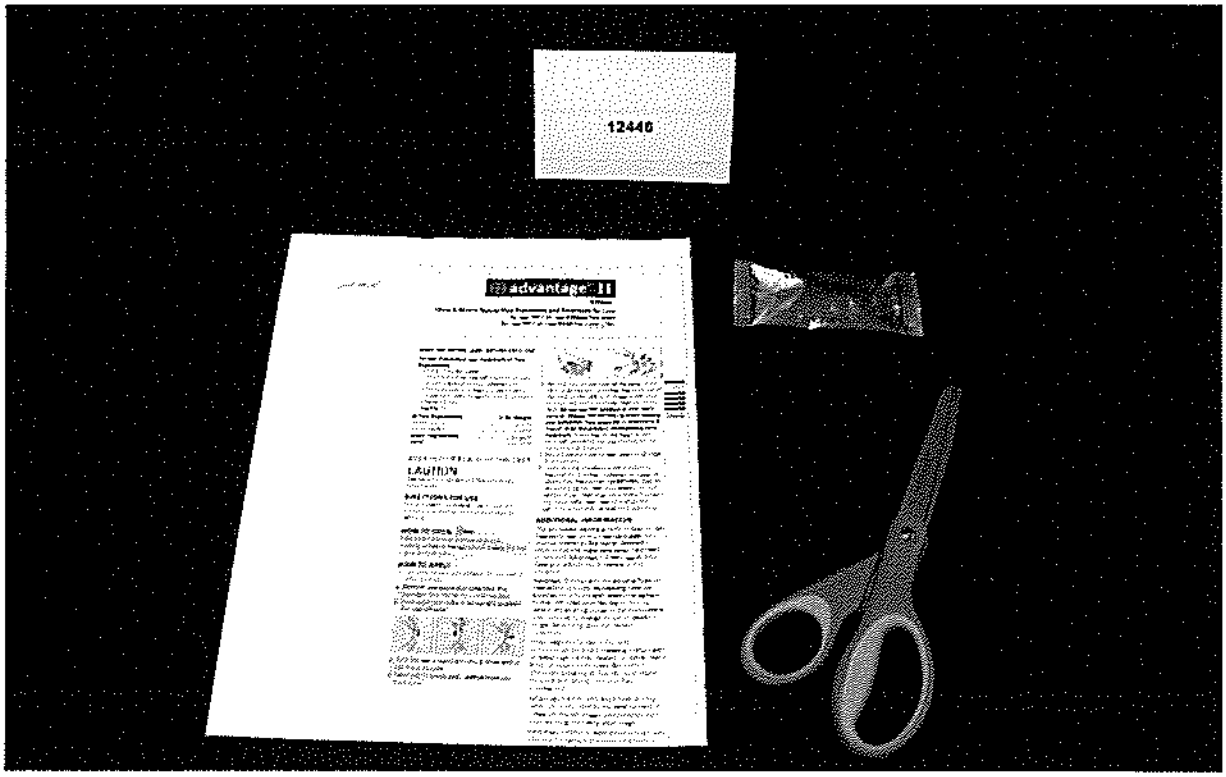
Bayer has conducted CRP testing of single pouches each one containing a 4-mL, 2.5-mL, 1-mL, 0.8-mL, 0.4-mL, or 0.23-mL tube. The first 4 sizes will continue to be marketed for use in dogs and the last three sizes will continue to be marketed for use in cats. Please note, 0.4-mL size is common for both dogs and cats. Therefore, the CRP testing of single pouches made from 12/12/40 aluminum foil type or 23/12/50 aluminum foil type for all sizes of the product would include for each foil type 6 CRP studies (i.e., 6 child panels + 6 senior adult panels) for the dogs and cats. As a guideline requirement for the CRP testing, all plastic tubes were filled with appropriate fill volume of pure water.

The package specifications, identification details, and photographs for the package tested are presented in Appendix 3.

Child-Resistant Packaging (CRP) Senior Adult Panel Test of 0.23mL Advantage® II Tube in Pouch Foil 12/12/40

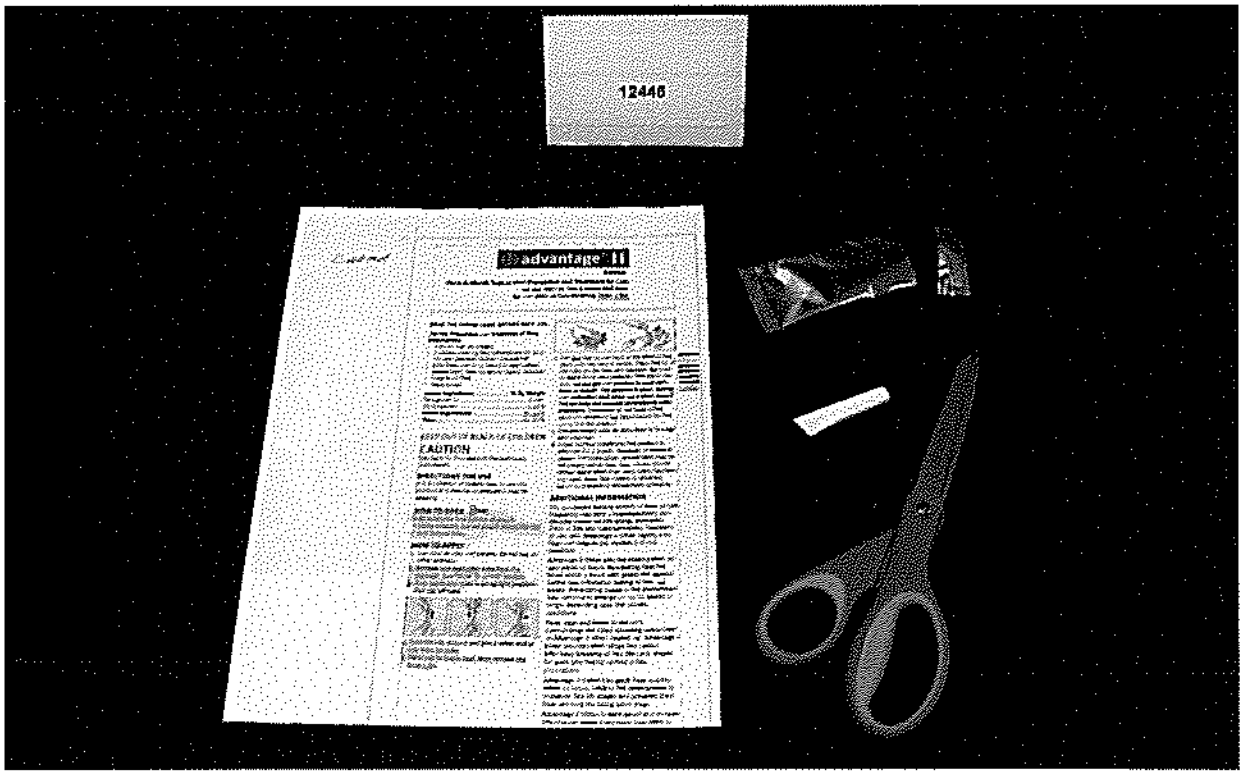
Great Lakes Marketing Research (GLM) conducted a senior adult panel test of 0.23mL Advantage® II Tube in Pouch Foil 12/12/40, Batch No. KP07V7B, using a panel of 100 seniors aged 50-70. The test protocol prescribed in the Federal Register, Title 16, Part 1700.20 was followed.

Photographs



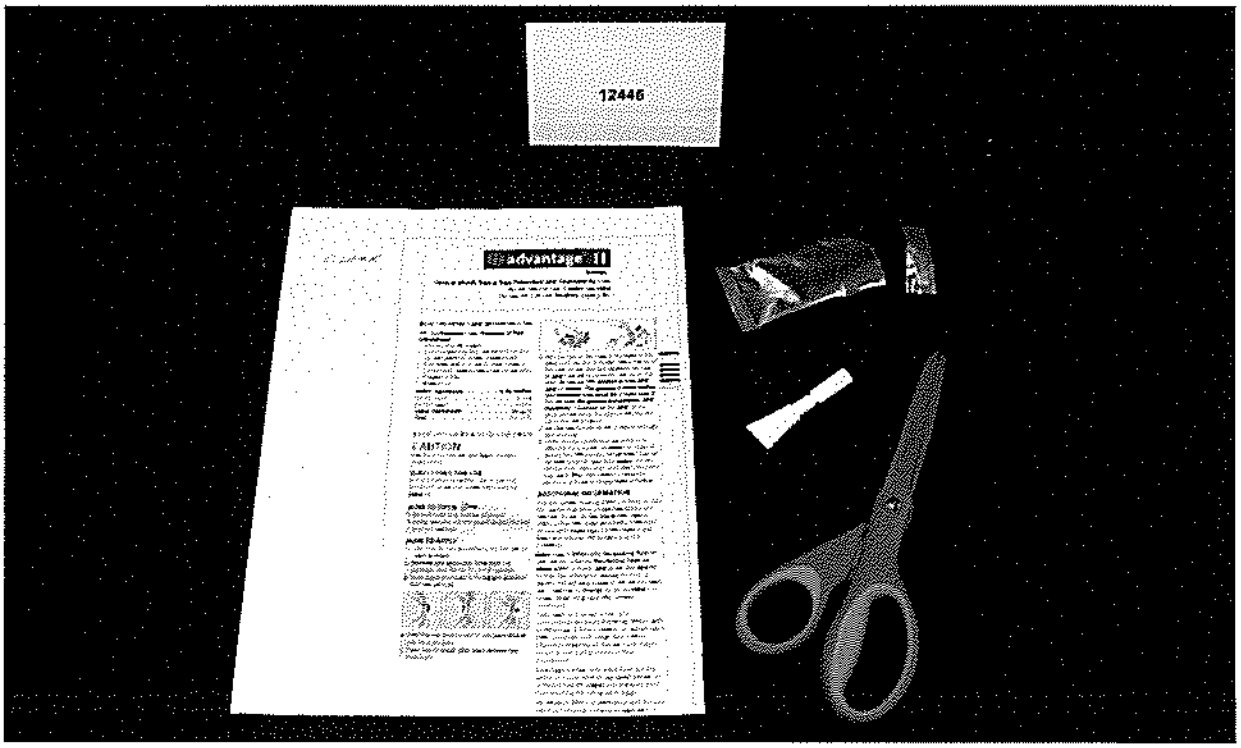
The pouch (12/12/40), opening instructions, and a pair of scissors presented to the senior adults for testing (GLM Project No. 12446).

Photographs



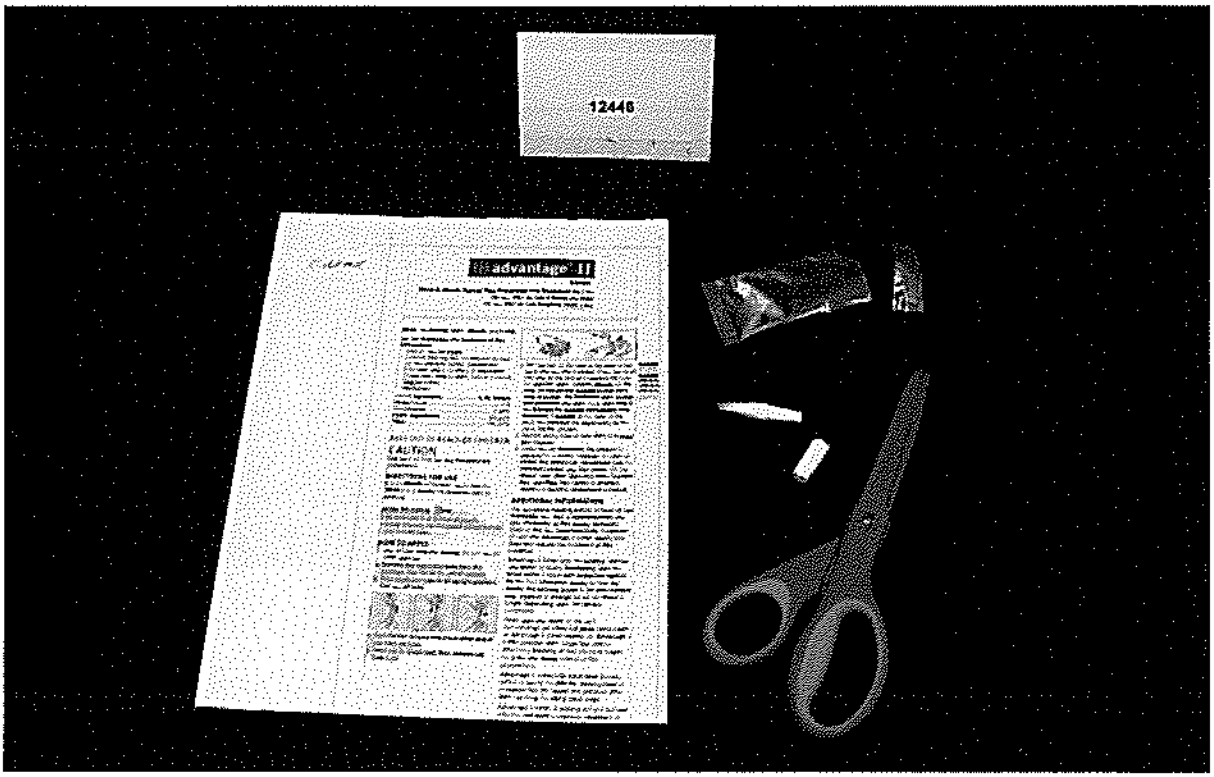
The pouch (12/12/40) as opened by the senior adult and the 0.23mL tube removed (GLM Project No. 12446).

Photographs



The 0.23mL tube as opened by the senior adult with the cap reversed to break the seal (GLM Project No. 12446).

Photographs



The cap removed from the 0.23mL tube by the senior adult to empty the contents in a plastic cup (GLM Project No. 12446).

Bayer HealthCare
Animal Health

Via Federal Express

December 12, 2012

Document Processing Desk (NO REGFEE – Additional Information)
Office of Pesticide Programs (7504P)
U.S. Environmental Protection Agency
Room S-4900, One Potomac Yard
2777 South Crystal Drive
Arlington, VA 22202-4501

Bayer HealthCare LLC
Animal Health
P.O. Box 390
Shawnee Mission, KS 66201-0390

Attention: Ms. Venus Eagle (PM01)
Registration Division

Subject: Advantage II Kitten
(EPA Reg. No. 11556-150)
Child-Resistant Packaging Certification

Dear Ms. Eagle:

I certify that the packaging (aluminum foil pouch; material# 01446067; PET/AL/PE 12/12/40) that will be used for this product meets the standard of 40 CFR 157.32.

Sincerely,

Douglas A. Spilker. Ph. D.
Manager, EPA Regulatory Affairs
Doug.Spilker@Bayer.com

Pages 152-163*Claimed confidential by submitter*

21-Day Screen of Amendment
(Completed by Contractor)

21-day Expires on 1/9/13

Document Part Of: 11556-150
MRID, If Any: 490238

Content Screen: Recommended to Pass/Fail

11-3 Review: Passed/Failed/NA

Overall Status: Pass/Fail

Document returned to:

Steve Schaible

01

PRIA 2 – 21 Day Content Screen Review Worksheet

(EPA/OPP Use Only)

3/23/09

21 Day Screen Start Date: 12/19/12

Experts In-Processing Signature: MP Date 12/20/12 Fee Paid: Yes ✓

Division management contacted on issues No_____ Yes _____ Date _____

EPA Reg. Number: 11556-150	EPA Receipt Date: 12/19/12

	Items for Review			Yes	No	N/A*
1	**Application Form** (EPA Form 8570-1)(link to form) signed & complete including package type			X		
2	**Confidential Statement of Formula** all boxes completed, form signed, and dated (EPA Form 8570-4) (Link to form)				X	
	a) All inerts (link to http://www.epa.gov/opprd001/inerts/), including fragrances, approved for the proposed uses (see Footnote A)	yes	no			
3	**Certification with Respect to Citation of Data** (EPA Form 8570-34) (Link to form) completed and signed (N/A if 100% repack)			X		
	Certificate and data matrix consistent			X		
	If applicant is relying on data that are compensable, is the offer to pay statement included. (see Footnote B)	yes	no			
	If applicable, is there a letter of Authorization for exclusive use only.					
4	**Formulator's Exemption Statement** (EPA Form 8570-27) (Link to form) completed and signed (N/A if source is unregistered or applicant owns the technical)					X
5	**Data Matrix** (EPA Form 8570-35) (Link to form) both internal and external copies (PR 98-5) (Link to PR 98-5) completed and signed (N/A if 100% repack)			X		
		yes	no			
	a) Selective Method (Fee category experts use)	✓				
	b) Cite-All (Fee category experts use)					
	c) Applicant owns all data (Fee category experts use)					
6	**5 Copies of Label** (link to **http://www.epa.gov/oppfead1/labeling/lrm/**) **(Electronic labels on CD are encouraged and guidance is available)**(link to http://www.epa.gov/pesticides/regulating/registering/submissions/index.htm#labels)			X		

7	**Is the data package consistent with PR Notice 86-5** (link to PRN 86-5)	X		
8	**Notice of Filing (link to http://www.epa.gov/pesticides/regulating/tolerance_petitions.htm) included with petitions (link to http://www.epa.gov/pesticides/regulating/tolerances.htm)**			X
9	**If applicable for conventional applications, reduced risk rationale (link to http://www.epa.gov/opprd001/workplan/reducedrisk.html)**			X
10	**Required Data (link to http://www.epa.gov/pesticides/regulating/data_requirements.htm) and/or data waivers. See Footnote C.** a) List study (or studies) not included with application			

Comments:

Amendment Pass
11-03 Pass

FG

MRID 490238

* N/A – Not Applicable

Footnotes

A. During the 21 day initial content review, all CSFs will be reviewed to determine whether all inerts listed, including fragrances, are approved for the proposed uses. If an unapproved inert is identified, the applicant must either 1) resolve the inert issue by, for example, removing the inert, substituting it with an approved inert, submitting documentation that EPA approved the inert for the proposed pesticidal uses, correcting mistakes on the CSF, etc. or 2) provide the data to support OPP approval of the inert or 3) withdraw the application. Removing or substituting an inert ingredient will require a new CSF and may require submission of data. All information, forms, data and documentation resolving the inert issue must have been received by the Agency or the application withdrawn within the 21 day period, otherwise, the Agency will reject the application as described below.

To successfully complete this aspect of the 21 day initial content screen, applicants are **strongly encouraged** to verify that all inert ingredients have been approved for the application's uses **even if a product is currently registered** by consulting the inert Web

site [link to http://www.epa.gov/opprd001/inerts/lists.html] and if the inert is not approved, to obtain the necessary inert approval prior to submitting an application to register a pesticide product containing that inert ingredient. Some inert ingredients are no longer approved for food uses or certain types of uses. The name and/or CAS number on a CSF must match the name and CAS number on this web site. Simple typographical errors in the name or CAS number have resulted in processing delays.

If an inert is not listed on the inert ingredient web site and the applicant believes that the inert has been approved, the applicant should contact the Inert Ingredient Assessment Branch (IIAB) at inertsbranch@epa.gov and resolve the issue. Copies of the correspondence with IIAB resolving the issue should accompany the application. All new inerts except PIP inerts are reviewed by IIAB. The IIAB should also be contacted for any questions on what supporting data needs to be submitted for and the Agency's inert review process. Questions on PIP inerts should be directed to the Chief of Microbial Pesticides Branch [Link to http://www.epa.gov/oppbppd1/biopesticides/contacts_bppd.htm].

When a brand, trade, or proprietary name of an inert ingredient is listed on a CSF, additional information such as an alternate name of the inert, CAS number or other information [link to http://www.epa.gov/opprd001/inerts/tips.pdf] must also be included to enable the Agency to determine if it has been approved. Each component of an inert mixture (including a fragrance) must be identified. In some cases, the supplier of the mixture or fragrance may need to provide this information to the Agency. Prior to the Agency's receipt of an application, applicants must arrange with a proprietary mixture or fragrance supplier to provide the component information to the Agency or promptly upon EPA's request. If the inert ingredients in a proprietary blend (including fragrances) cannot or are not identified or provided within the 21-day content review period, the Agency will reject the application.

During the 21 day content review, applicants should submit information to the individual identified by the Agency when the applicant is informed of an unapproved inert.

Unapproved Inerts Identified on CSFs

All applications except conventional new products and PIPs

Once an unapproved inert is identified on a CSF, the Agency will contact the applicant with the following options:

1. Correct the application by, for instance, correcting the inert's identity or CAS number, providing documentation that the inert has been approved, or removing the unapproved inert from the CSF or replacing it with one that is approved for the application's uses; or

2. Submit the information and data needed for the Agency to approve the unapproved inert. If this option is selected and implemented, the Agency may request an extension in the PRIA decision review timeframe to accommodate the inert review/approval process;

3. Withdraw the application (the Agency retains 25% of the full fee for the fee category estimated); or

If none of these options is selected and implemented by the applicant within the 21 day content review period, the Agency will reject the application and retain 25% of the full fee of the category identified.

Conventional New Product Applications

When the Registration Division identifies an unapproved inert on a CSF with an application for a new product that the applicant has not identified as requiring an inert approval (R311, R312 or R313), it will contact the applicant with the following options:

1. Correct the application by, for instance, correcting the inert's identity or CAS number, providing documentation that the inert has been approved, or removing the unapproved inert from the CSF or replacing it with one that is approved for the application's uses; or

2. Submit the information and data needed for the Agency to approve the unapproved inert, including any required petition to establish or amend a tolerance or exemption from a tolerance. (This option may change the PRIA category for the application, which could require a longer decision review time and a larger fee. If additional fees are due, they must be received by the Agency within the 21 day content review period.)

3. Withdraw the application (the Agency retains 25% of the full fee for the fee category estimated); or

If none of the above options is selected and implemented during the 21-day content-review period, the Agency will reject the application and retain 25% of the appropriate fee for the new product-inert approval category.

PIP Applications

When the Biopesticide and Pollution Prevention Division identifies an unapproved inert on a PIP CSF and a request to approve the inert does not accompany the application, it will contact the applicant with the following options:

1. Correct the application by, for instance, correcting the spelling or name of the inert to that in 40 CFR 174, or providing documentation that the inert has been approved; or

2. Submit the information and data needed for the Agency to approve the unapproved inert. If an inert ingredient tolerance exemption petition is required, the petition must be received by the Agency and the B903 fee paid within the 21 day period. If this option is selected and implemented, the Agency will discuss harmonizing the timeframe for both actions.

3. Withdraw the application (the Agency retains 25% of the full fee for the fee category estimated); or

If none of the above options is selected and implemented during the 21 day content review period, the Agency will reject the application and retain 25% of the fee.

B. A policy on documentation of offers to pay is still being developed, however, for a me-too or fast track (similar/identical) new product, R300 or A530, an application without the necessary authorizations of offers to pay will be placed into either R301 or A531. The Agency recommends that authorizations of offers to pay be submitted with other PRIA applications to avoid delays in the Agency's decision.

C. Biopesticide applicants are advised to contact the Agency and discuss study waivers prior to submitting their application to the Agency. Documentation of such discussions should be submitted with the study waiver.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

December 20, 2012

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

OPP Decision Number: D-473308
EPA File Symbol or Registration Number: 11556-150
Product Name: ADVANTAGE II KITTEN
EPA Receipt Date: 19-Dec-2012
EPA Company Number: 11556
Company Name: BAYER HEALTHCARE LLC

DOUGLAS SPILKER
BAYER HEALTHCARE LLC
ANIMAL HEALTH DIVISION
PO Box 390
SHAWNEE MISSION, KS 66201-0390

SUBJECT: Receipt of Registration Amendment Subject to Registration Service Fee

Dear Registrant:

The Office of Pesticide Programs has received your amendment and certification of payment. If you submitted data with this application, the results of the PRN-2011-3 screen will be communicated separately. During the administrative screen, the Office of Pesticide Programs has determined that this Action is subject to a Pesticide Registration Service Fee as defined in the Pesticide Registration Improvement Act.

The Action has been identified as Action Code: R340

AMENDMENT;NON-FAST TRACK;REVIEW WITHIN RD, E.G. PRECAUTIONARY LABELING;

No additional payment is due at this time.

If you have any questions, please contact the Pesticide Registration Service Fee Ombudsman at (703) 308-9362.

Sincerely,

Front End Processing Staff
Information Technology & Resources Management Division

Fee for Service

{928375F~

This package includes the following

- ○ New Registration
- ◉ Amendment

☑ Studies? ☐ Fee Waiver?

☐ volpay % Reduction: ___

for Division

- ○ AD
- ○ BPPD
- ◉ RD

Risk Mgr. 1

Receipt No. S- 928375

EPA File Symbol/Reg. No. 11556-150

Pin-Punch Date: 12/19/2012

This item is NOT subject to FFS action.

Action Code:

Requested: R340

Granted: R340

Amount Due: $ 3017.00

Parent/Child Decisions:

☐ Inert Cleared for Intended Use ☐ Uncleared Inert in Product

Reviewer: KV Mary Date: 12-20-12

Remarks:

Doug Spilker

From: paygovadmin@mail.doc.twai.gov
Sent: Thursday, December 13, 2012 8:01 AM
To: Doug Spilker
Subject: Pay.gov Payment Confirmation: PRIA Service Fees

Your payment has been submitted to Pay.gov and the details are below. If you have any questions regarding this payment, please contact Pay.gov Customer Service by phone at (800) 624-1373 or by email at pay.gov.clev@clev.frb.org.

Application Name: PRIA Service Fees
Pay.gov Tracking ID: 258TIMK3
Agency Tracking ID: 74387643012
Transaction Type: Sale
Transaction Date: Dec 13, 2012 9:00:50 AM

Account Holder Name: Douglas A. Spilker
Transaction Amount: $3,617.00
Billing Address: 12707 Shawnee Mission Parkway
City: Shawnee
State/Province: KS
Zip/Postal Code: 66216
Country: USA
Card Type: MasterCard
Card Number: **********0576

Decision Number:
Registration Number: 11556-150
Company Name: Bayer HealthCare LLC, AH
Company Number: 115S6
Action Code: R340

THIS IS AN AUTOMATED MESSAGE. PLEASE DO NOT REPLY.

Memorandum

Date: 12/26/12

To: RM 01, Regulatory Manager

From: Information Services Branch, ITRMD

Your receipt of this data submission is not an indication that MRIDs for the enclosed studies have been posted to OPPIN.

We expect that it will be approximately 5 days from the above date before the study-level data is available in OPPIN.

If you have any questions about this process, please contact Teresa Downs (305-5363).

This is a:
- [X] fully accepted submission
- [ ] partially accepted submission
- [ ] rejected submission

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

December 26, 2012

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

BAYER HEALTHCARE LLC
PO.BOX : 390
SHAWNEE MISSION, KS 66201-0390

Report of Analysis for Compliance with PR Notice 11-03

Thank you for your submittal of 19-DEC-12. Our staff has completed a preliminary analysis of the material. The results are provided as follows:

Your submittal was found to be in full compliance with the standards for submission of data contained in PR Notice 11-03. A copy of your bibliography is enclosed, annotated with Master Record ID's (MRIDs) assigned to each document submitted. Please use these numbers in all future references to these documents. Thank you for your cooperation. If you have any questions concerning this data submission, please raise them with the cognizant Product Manager, to whom the data have been released.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
CHEMICAL SAFETY AND
POLLUTION PREVENTION

JAN 10 2013

Dr. Douglas A. Spilker
Bayer Healthcare LLC
Animal Health Division
P.O. Box 390
Shawnee Mission, KS 66201-0390

Subject: Notice of Extension of Conditional Registrations until January 17, 2015

Dear Dr. Spilker:

This letter is in reference to your applications dated November 28, 2012, in which you request to extend the following, conditional registrations:

Advantage II Medium Dog	EPA Reg. No. 11556-125
Advantage II Large Dog	EPA Reg. No. 11556-127
Advantage II Small Dog	EPA Reg. No. 11556-128
Advantage II Extra Large Dog	EPA Reg. No. 11556-130
Advantage II Kitten	EPA Reg. No. 11556-150
Advantage II Small Cat	EPA Reg. No. 11556-151
Advantage II Large Cat	EPA Reg. No. 11556-152

The above-referenced registrations contain conditions calling for the registrations to expire two years from the date the products are first released for shipment (i.e., January 17, 2013). Additionally, Bayer is required to adhere to the spot on label mitigation, and to submit quarterly enhanced incident reports and quarterly sales information for each of the above registrations.

The Agency has found Bayer to be in compliance with the terms and conditions for the subject products, and is therefore is granting the request to extend the 2-year time-limited registration restrictions. As such, the following changes are being made to the terms and conditions for the products listed above:

- **The 2-year time-limited registration restrictions have been extended for an additional 2 years. The new expiration dates for the registrations listed above are January 17, 2015.**

Please note that these products are still subject to all other previously required conditions of registration. If Bayer wishes to remove the time limitations altogether, please submit to the Product Manager an amendment application for each product to change the terms and conditions of the registration. Please include with your submission a written rationale for the removal of the time limitation. As you remember, the Agency included this time limitation as a condition of registration for your products to allow for the post-market surveillance[1] of these products. Therefore, we recommend that you include in your rationale the following information, along with any additional information or analyses you think would be helpful to the agency (e.g., tables, charts, information on stewardship activities, etc…):

- A summary and analysis of the incidents received associated with these products, including information on the following:
  - A comprehensive analysis of incident rates per doses distributed;
  - An analysis of historical incident trends since the products' release into the marketplace;
  - An analysis of historical incident trends by weight range of animal, breed, weight range of product, etc…
- If these products are also registered in the European Union or Canada, information on incident rates per doses distributed and trends in those countries.

Please also note that requests to remove the expiration date condition are not subject to PRIA fees and do not have to be submitted under PRIA. However, these would also not be considered 90-day, fast-track submissions in order to allow the EPA enough time to fully evaluate the information provided. After receiving these submissions, the EPA will consider the incidents received since the initial registration; review the information and rationale provided; and make a decision on the request.

If you have any questions, please contact the product manager, Venus Eagle, at eagle.venus@epa.gov or (703) 308-8045.

Regards,

Venus Eagle for

Meredith Laws, Chief
Insecticide-Rodenticide Branch
Registration Division (7505P)

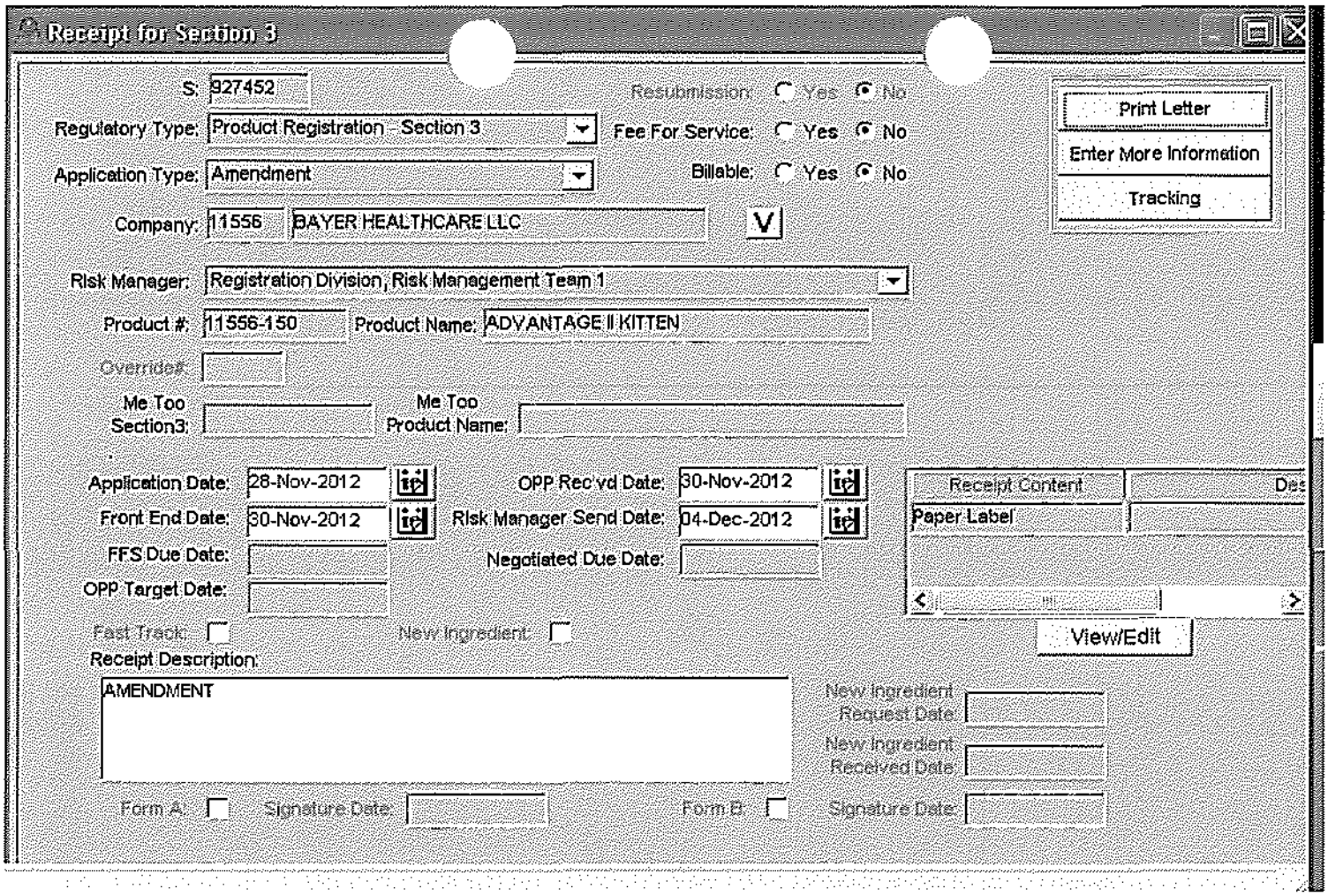
[1] http://www.epa.gov/pesticides/health/spot-on-meetings.html

FAST-TRACK AMENDMENTS – Completeness Screening Checklist

Expert's In-Processing Signature: KVNDN Date: 12-6-12 PM #: 1

EPA Reg. Number: 11556 -150 -151 -152	EPA Receipt Date: 11-30-12

	Checklist Item	Yes	No	N/A
1	**Application Form** (EPA Form 8570-1) - signed?	✓		
2	**Confidential Statement of Formula** (EPA Form 8570-29) - signed?			
3	**Certification with Respect to Citation of Data** (EPA Form 8570-34) - signed?			
4	**Formulator's Exemption Statement** (EPA Form 8570-27) - signed?			
5	**Data Matrix** (EPA Form 8570-35) [Applicable for adding me-too uses] - signed?			
	a) Selective Method?			
	b) Cite-All Method?			
	c) Public copy of Matrix provided? See PR Notice 98-5			
6	**Is Label included?** (5 copies)	✓		
	a) Electronic Label submitted?		✓	
	Comments: Set of 3			


Receipt for Section 3
S: 927452
Resubmission: Yes No
Regulatory Type: Product Registration - Section 3
Fee For Service: Yes No
Application Type: Amendment
Billable: Yes No
Company: 11556 BAYER HEALTHCARE LLC
Print Letter
Enter More Information
Tracking
Risk Manager: Registration Division, Risk Management Team 1
Product #: 11556-150
Product Name: ADVANTAGE II KITTEN
Override#:
Me Too Section3:
Me Too Product Name:
Application Date: 28-Nov-2012
OPP Received Date: 30-Nov-2012
Front End Date: 30-Nov-2012
Risk Manager Send Date: 04-Dec-2012
FFS Due Date:
Negotiated Due Date:
OPP Target Date:
Receipt Content
Paper Label
View/Edit
Fast Track:
New Ingredient:
Receipt Description:
AMENDMENT
New Ingredient Request Date:
New Ingredient Received Date:
Form A:
Signature Date:
Form B:
Signature Date:

UNIT[illegible]ATES ENVIRONMENTAL PROTECTI[illegible]GENCY
WASHINGTON, D.C. 20460

December 4, 2012

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

DR. BRUCE MARTIN
BAYER HEALTHCARE LLC
ANIMAL HEALTH DIVISION
PO Box 390
SHAWNEE MISSION, KS 66201-0390

PRODUCT NAME: ADVANTAGE II KITTEN
COMPANY NAME: BAYER HEALTHCARE LLC
OPP IDENTIFICATION NUMBER:
EPA FILE SYMBOL: 11556-150
EPA RECEIPT DATE: 11/30/12

SUBJECT: RECEIPT OF AMENDMENT

DEAR REGISTRANT:

The Office of Pesticide Programs has received your application for an amendment and it has passed an administrative screen for completeness.

During the initial screen we determined that the application appears to qualify for fast track review. The package will now be forwarded to the Product Manager for review to determine its acceptability for fast track status.

If you have any questions, please contact Registration Division, Risk Management Team 1, at (703) 308-8045.

Sincerely,

Front End Processing Staff
Information Services Branch
Information Technology & Resources Management Division

Bayer HealthCare
Animal Health

Via Federal Express

November 28, 2012

Document Processing Desk (Non-PRIA Action)
Office of Pesticide Programs (7505P)
U.S. Environmental Protection Agency
Room S-4900, One Potomac Yard
2777 South Crystal Drive
Arlington, VA 22202-4501

Attention: Ms. Venus Eagle/PM 01

Bayer HealthCare LLC
Animal Health
P.O. Box 390
Shawnee Mission, KS 66201-0390

Subject: ***Request for Extension of Time-limited Registrations for the following products:***
Advantage II Kitten (EPA Reg. No. 11556-150)
Advantage II Small Cat (EPA Reg. No. 11556-151)
Advantage II Large Cat (EPA Reg. No. 11556-152)

Dear Ms. Eagle:

Reference is made to the current registrations of the subject products, and the Agency's letter to us, dated September 20, 2011 (received October 11, 2011), regarding "Implementation of Label Changes to Pet Spot-on Products." In that letter, certain actions were required by us, the registrant, to maintain these registrations. These registrations were designated as "Time-limited" with an **expiration date of January 17, 2013.** Since we have complied with the conditions of the aforementioned Agency letter, we request an extension of these registrations, until such time as to allow us to pursue the complete removal of the time limitations.

The Agency has now accepted draft labeling for Advantage II Kitten (dated 09/25/2012), for Advantage II Large Cat (dated 9/25/12) and Advantage II Small Cat (dated 11/07/12) with the appropriate revisions outlined in the aforementioned EPA "Implementation" letter, and subsequent requests of the Agency. Also as required, we submitted the respective printer's proofs of each of the elements of the Final Printed Labeling (packaging) for these products.

Furthermore, we have submitted the required quarterly enhanced incident reports for these products beginning with the products' initial releases for shipment (6 quarters). Adverse incident reports have been and continue to be monitored in accordance to the stipulations of the conditional registration. Analysis of the accumulated incident reporting for the initial eighteen (18) months of commercial distribution of the Advantage II Cat registrations indicate occurrence rates to range from rare to very rare. Actual rates (expressed as the ratio incident : doses sold) were 1:7,249, 1:10,924 and 1:8,440 for the Kitten, Small Cat and Large Cat respectively.

Since we have complied with the conditions of the aforementioned Agency's letter to us, dated September 20, 2011, we request an extension of these registrations as soon as possible, since these registrations have an **expiration date of January 17, 2013.** Enclosed are additional draft copies of the EPA stamped-accepted labels for these products (only the internal version code and date of draft has changed) for your use in processing this request.

In a separate submission, we will be provide an analysis of the submitted enhanced incident reports of these products showing that there is no longer a need for these products to have time-limited registrations based on the safe use history of these products on the respective companion animals.

If you have any questions, please do not hesitate to call (913-268-2751).

Sincerely,

Douglas A. Spilker. Ph. D.
Manager, EPA Regulatory Affairs
Doug.Spilker@Bayer.com

Enclosures:

1) Advantage II Kitten - Application
2) Advantage II Kitten - Draft label, dated 11/28/12 (1 copy)
3) Advantage II Small Cat - Application
4) Advantage II Small Cat - Draft label, dated 11/28/12 (1 copy)
5) Advantage II Large Cat - Application
6) Advantage II Large Cat - Draft label, dated 11/28/12 (1 copy)

Please read instructions on reverse before completing form.

Form Approved. OMB No. 2070-0060

United States
Environmental Protection Agency
Washington, DC 20460

[ ] Registration
[X] Amendment
[ ] Other

OPP Identifier Number

Application for Pesticide - Section I

1. Company/Product Number	2. EPA Product Manager	3. Proposed Classification
11556-150	Venus Eagle	[X] None [ ] Restricted
4. Company/Product (Name)	**PM#**	
Advantage II Kitten	01	

5. Name and Address of Applicant *(Include ZIP Code)*

Bayer Healthcare LLC, Animal Health Division
P.O. Box 390
Shawnee Mission, KS 66201-0390

[ ] *Check if this is a new address*

6. Expedited Review. In accordance with FIFRA Section 3(c)(3)(b)(ii, my product is similar or identical in composition and labeling to:

EPA Reg. No. _____

Product Name _____

Section - II

[X] Amendment - Explain below.
[ ] Resubmission in response to Agency letter dated _____
[ ] Notification - Explain below.
[ ] Final printed labels in response to Agency letter dated _____
[ ] "Me Too" Application.
[ ] Other - Explain below.

Explanation: Use additional pages if necessary. (For section I and Section II.)

Non-PRIA Action: Bayer has complied with the conditions of the Agency's letter, dated September 20, 2011, and therefore requests a time extension of this registration as soon as possible, since it has an expiration date of January 17, 2013. Enclosed is a draft copy of the EPA stamped-accepted label for this product (only the internal version code and date of draft has changed) for your use in processing this request. Please see cover letter of 11/28/12 for more details. Email Contact: doug.spilker@bayer.com

Section - III

1. Material This Product Will Be Packaged In:

Child-Resistant Packaging	Unit Packaging	Water Soluble Packaging	2. Type of Container
[ ] Yes [ ] No	[ ] Yes [ ] No	[ ] Yes [ ] No	[ ] Metal [ ] Plastic [ ] Glass [ ] Paper [ ] Other (Specify)
* ***Certification must be submitted***	If "Yes" Unit Packaging wgt. / No. per container	If "Yes" Package wgt / No. per container	

3. Location of Net Contents Information	4. Size(s) Retail Container	5. Location of Label Directions
[ ] Label [ ] Container		[ ]

6. Manner in Which Label is Affixed to Product: [ ] Lithograph [ ] Paper glued [ ] Stenciled [ ] Other _____

Section - IV

1. Contact Point *(Complete items directly below for identification of individual to be contacted, if necessary, to process this application.)*

Name	Title	Telephone No. (Include Area Code)
Douglas A. Spilker, Ph.D.	Manager, EPA Reg. Affairs	913-268-2751

Certification

I certify that the statements I have made on this form and all attachments thereto are true, accurate and complete. I acknowledge that any knowingly false or misleading statement may be punishable by fine or imprisonment or both under applicable law.

6. Date Application Received (Stamped)

2. Signature	3. Title
Douglas A. Spilker	Manager, EPA Reg. Affairs
4. Typed Name	**5. Date**
Douglas A. Spilker, Ph.D.	28 Nov. 2012

EPA Form 8570-1 (Rev. 3-94) Previous editions are obsolete. White - EPA File Copy (original) Yellow - Applicant Copy

Material Sent for Data Extraction

Reg. # 11556-150

Description: _____

☐ Material(s) Sent to Data Extraction Contractors:

- ☑ New Stamped Label Dated 10/25/12
- ☐ Notification Dated _____
- ☐ New CSF(s) Dated _____
- ☐ Other: _____

☐ Decision #: _____

☐ Other Action/Comments: _____

_____

File this coversheet and attached materials in the jacket. It must be well organized and clipped together, NOT STAPLED. Then give the jacket with the coversheet and materials to staff in the Information Services Center (ISC) (Room S-4900). If a jacket is full or only available as an image, please file materials in a new jacket and bring it down to the (ISC). For further information please call 703-605-0716.

Reviewer: Autumn Metzger

Phone: 305-5314 Division: RD - IRB

Date: 12/27/12

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OCT 2 5 2012

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

Douglas Spilker, Ph.D
Bayer HealthCare LLC, Animal Health Division
P.O. Box 390
Shawnee Mission, KS 66201-0390

Dear Dr. Spilker:

Subject: Amendment to update labels per spot on mitigation letter sent by the Agency dated September 30, 2011
EPA Registration Nos./Product name:
11556-150, Advantage II Kitten ✓
11556-151, Advantage II Small Cat
11556-152, Advantage II Large Cat

The labeling referred to above submitted in connection with the Federal Insecticide, Fungicide and Rodenticide, as amended are acceptable.

As a reminder, **this registration is time-limited and expires January 17, 2013.** You must apply to extend the expiration and/or to change the terms of this registration.

Per the implementation of label changes for pet spot on products, the Agency has reviewed a copy of the print ready label

A stamped copy of the labeling is enclosed for your records. If you have any questions regarding this label, please contact Autumn Metzger at (703) 305-5314.

Sincerely,

Venus Eagle

Venus Eagle
Product Manager 01
Insecticide-Rodenticide Branch
Registration Division (7505P)

Reason To Issue:	Revise according to EPA "Implementation of Label Changes to Pet Spot-On Products" document	Date: 09/25/12 Supersedes: 03/26/12 and 09/15/10

NOTE TO REVIEWER: [(Brackets and parentheses indicate alternate language)]

[Front Panel]

Advantage® II Kitten

Once-A-Month Topical Flea Prevention and Treatment for Cats
For Use ONLY on Cats 8 Weeks and Older and Weighing 2 – 5 lbs.

[Selected optional claims bulleted here from page 10 and/or 11]

-
-
-
-

Active Ingredients	% By Weight
Imidacloprid	9.10%
Pyriproxyfen	0.46%
Other Ingredients	90.44%
Total	100.00%

EPA Est. No. 11556-XXX-X EPA Reg No. 11556-150

KEEP OUT OF REACH OF CHILDREN

CAUTION

See back panel for Precautionary Statements.
For Directions for Use, Storage and Disposal, and First Aid see package insert inside.

ACCEPTED
OCT 2 5 2012
Under the Federal Insecticide, Fungicide, and Rodenticide Act, as amended, for the pesticide registered under:
EPA. Reg. No: 11556 – 150

Reason To Issue:	Revise according to EPA "Implementation of Label Changes to Pet Spot-On Products" document	Date: Supersedes:	09/25/12 03/26/12 and 09/15/10

[Back Panel]

Advantage® II Kitten

Once-A-Month Topical Flea Prevention and Treatment for Cats
For Use ONLY on Cats 8 Weeks and Older and Weighing 2 - 5 lbs.

READ THE ENTIRE LABEL BEFORE EACH USE
For the Prevention and Treatment of Flea Infestations

PRECAUTIONARY STATEMENTS

HAZARDS TO HUMANS

CAUTION: Harmful if swallowed. Causes moderate eye irritation. Avoid contact with eyes or clothing. Wash hands thoroughly with soap and warm water after handling. Keep out of reach of children. Do not contaminate feed or food.

HAZARDS TO DOMESTIC ANIMALS

For external use only. Do not apply to cats or kittens under 8 weeks of age or weighing less than 2 lbs. As with any product, consult your veterinarian before using this product on debilitated, aged, pregnant or nursing cats. Individual sensitivities, while rare, may occur after using ANY pesticide product for cats. If signs persist, or become more severe, consult a veterinarian immediately. If your cat is on medication, consult your veterinarian before using this or any other product.

Side Effects: Monitor your cat after application. Side effects, although very rare, may include signs of skin irritation such as redness, scratching, or other signs of discomfort. Gastrointestinal signs such as hypersalivation, vomiting or diarrhea have also been reported. If these or other side effects (such as lethargy) occur, consult your veterinarian or call 1-800-422-9874.

For consumer questions call 1-800-255-6826.
For medical emergencies call 1-800-422-9874.

RESTRICTIONS:

- Use only on cats or kittens 8 weeks and older. Do not apply to cats or kittens weighing less than 2 lbs. Do not use on other animals.
- Do not apply more than one (1) tube per treatment.
- Do not have contact or allow children to have contact with treated area until completely dry.

Reason To Issue:	Revise according to EPA "Implementation of Label Changes to Pet Spot-On Products" document	Date:	09/25/12
		Supersedes:	03/26/12 and 09/15/10

Net Contents: [X] Tube(s), each 0.0078 fl. oz. (0.23 mL)

[Sample - Not for (Re)Sale]

Manufactured For

Bayer HealthCare LLC
Animal Health Division
P.O. BOX 390
Shawnee Mission, Kansas 66201 USA

Made in Germany

[Back Panel and/or Insert]

Advantage® II Kitten

Once-A-Month Topical Flea Prevention and Treatment for Cats
For Use ONLY on Cats 8 Weeks and Older and Weighing 2 - 5 lbs.

READ THE ENTIRE LABEL BEFORE EACH USE
For the Prevention and Treatment of Flea Infestations

DIRECTIONS FOR USE

It is a violation of Federal Law to use this product in a manner inconsistent with its labeling.

HOW TO OPEN

1. Being careful not to cut close to the blister cavities, take scissors and cut off one section of the card containing a single tube.
2. Take the separated section, and cut into the blister cavity across the small side, close to the cap of the tube.
3. Peel off the foil, and take out the tube.
4. Repeat steps 1 to 3 for each tube.

HOW TO APPLY

1. Remove one applicator tube from the package. See "HOW TO OPEN" section.

2. Hold applicator tube in an upright position facing away from you and your pet's face and eyes. Pull cap off tube.

[Visuals Depicting How to Open Applicator Tube]

3. Turn the cap around and place other end of cap back on tube.

4. Twist cap to break seal, then remove cap from tube.

5. Part the hair on the neck at the base of the skull until the skin is visible. Place the tip of the tube on the skin and squeeze the tube to expel the entire contents directly on the skin. *Do not get this product in your cat's eyes, or allow your cat to ingest this*

product. The product is bitter tasting and salivation may occur for a short time if the cat licks the product immediately after treatment. Treatment at the base of the skull will minimize the opportunity for the cat to lick the product. Do not allow the product to run off.

[Visuals Depicting Application to Animal]

6. Discard empty tube as described in Storage and Disposal.

7. Under normal conditions this product is effective for a month. However, in case of severe flea infestation, retreatment may be necessary earlier than four (4) weeks. Do not retreat more often than once every fourteen (14) days. After flea control is attained, return to a monthly retreatment schedule.

PRODUCT INFORMATION

The successive feeding activity of fleas on cats frequently elicits a hypersensitivity skin disorder known as flea allergy dermatitis (FAD) or flea bite hypersensitivity. Treatment of cats with Advantage® II Kitten kills fleas and may reduce the incidence of this condition.

Advantage® II Kitten kills the existing fleas on cats within 12 hours. Reinfesting fleas are killed within 2 hours with protection against further flea infestation lasting for up to four (4) weeks. Pre-existing pupae in the environment may continue to emerge for six (6) weeks or longer depending upon the climatic conditions.

Fleas, eggs and larvae in the cat's surroundings are killed following contact with an Advantage® II Kitten treated cat. Advantage® II Kitten provides multi-stage flea control effectively breaking all flea life-cycle stages for lasting control of flea populations.

Advantage® II Kitten kills adult fleas quickly, within 12 hours, inhibits the development of immature flea life stages and prevents them from reaching the biting adult stage.

Advantage® II Kitten is waterproof and remains effective following a shampoo treatment or after exposure to rain or sunlight.

Apply monthly treatments for optimal control and prevention of fleas.

Reason To Issue:	Revise according to EPA "Implementation of Label Changes to Pet Spot-On Products" document	Date: Supersedes:	09/25/12 03/26/12 and 09/15/10

KEEP OUT OF REACH OF CHILDREN

CAUTION

PRECAUTIONARY STATEMENTS
HAZARDS TO HUMANS

CAUTION: Harmful if swallowed. Causes moderate eye irritation. Avoid contact with eyes or clothing. Wash hands thoroughly with soap and warm water after handling. Keep out of reach of children. Do not contaminate feed or food.

FIRST AID	
If Swallowed:	• Call a poison control center or doctor immediately for treatment advice. • Have person sip a glass of water if able to swallow. • Do not induce vomiting unless told to do so by the poison control center or doctor. • Do not give anything to an unconscious person.
If In Eyes:	• Hold eye open and rinse slowly and gently with water for 15-20 minutes. Remove contact lenses, if present, after the first 5 minutes, then continue rinsing eye. • Call a poison control center or doctor for treatment advice.
If On Skin	• Wash with plenty of soap and water.
HOT LINE NUMBER	
Have the product container or label with you when calling a poison control center or doctor, or going for treatment. For medical emergencies call 1-800-422-9874. For customer questions call 1-800-255-6826.	
NOTE TO PHYSICIAN	
Treat the patient symptomatically.	

HAZARDS TO DOMESTIC ANIMALS

For external use only. Do not apply to cats or kittens under 8 weeks of age or weighing less than 2 lbs. As with any product, consult your veterinarian before using this product on debilitated, aged, pregnant or nursing cats. Individual sensitivities, while rare, may occur after using ANY pesticide product for cats. If signs persist, or become more severe, consult a veterinarian immediately. If your cat is on medication, consult your veterinarian before using this or any other product.

Side Effects: Monitor your cat after application. Side effects, although very rare, may include signs of skin irritation such as redness, scratching, or other signs of discomfort. Gastrointestinal signs such as hypersalivation, vomiting or diarrhea have also been reported. If these or other side effects (such as lethargy) occur, consult your veterinarian or call 1-800-422-9874.

For consumer questions call 1-800-255-6826.
For medical emergencies call 1-800-422-9874.

RESTRICTIONS:

- Use only on cats or kittens 8 weeks and older. Do not apply to cats or kittens weighing less than 2 lbs. Do not use on other animals.
- Do not apply more than one (1) tube per treatment.
- Do not have contact or allow children to have contact with treated area until completely dry.

STORAGE AND DISPOSAL

Do not contaminate water, food or feed by storage or disposal.

Pesticide Storage: Store in a cool, dry place inaccessible to children and pets. **Pesticide Disposal and Container Handling:** Nonrefillable container. **If empty**: Do not reuse or refill this container. Place in trash or offer for recycling if available. **If partly filled**: Call your local solid waste agency or 1-800-422-9874 for disposal instructions. Never place unused product down any indoor or outdoor drain.

LIMITED WARRANTY AND LIMITATION OF DAMAGES

Bayer HealthCare LLC, Animal Health Division warrants that this material conforms to the chemical description on the label. TO THE EXTENT CONSISTENT WITH APPLICABLE LAW, BAYER MAKES NO OTHER EXPRESS OR IMPLIED WARRANTY, INCLUDING ANY OTHER EXPRESS OR IMPLIED WARRANTY OF FITNESS OR MERCHANTABILITY, and no agent of Bayer is authorized to do so except in writing with a specific reference to this warranty. Any damages arising from a breach of this warranty shall be limited to direct damages and shall not include consequential commercial damages such as loss of profits or values, etc.

Reason To Issue:	Revise according to EPA "Implementation of Label Changes to Pet Spot-On Products" document	Date:	09/25/12
		Supersedes:	03/26/12 and 09/15/10

[Label on Individual Tube]

Advantage® II Kitten

9.10% Imidacloprid

0.46% Pyriproxyfen

0.0078 fl. oz. (0.23 mL)

EPA Reg. No. 11556-150

Keep Out of Reach of Children

CAUTION

Read The Entire Label Before Use

BAYER

Lot No. 0000000

Reason To Issue:	Revise according to EPA "Implementation of Label Changes to Pet Spot-On Products" document	Date: Supersedes:	09/25/12 03/26/12 and 09/15/10

[Label on blister card; one card containing 1, 2, 3, 4, 5, or 6 tubes]

Advantage® II Kitten

For external use only on cats and kittens 8 weeks and older and weighing 2 -5 lbs.

9.10% Imidacloprid

0.46% Pyriproxyfen

[X] - 0.0078 fl. oz. (0.23 mL)

EPA Reg. No. 11556-150

BAYER

Reason To Issue:	Revise according to EPA "Implementation of Label Changes to Pet Spot-On Products" document	Date: 09/25/12 Supersedes: 03/26/12 and 09/15/10

NOTE TO REVIEWER: [(Brackets and parentheses indicate alternate language)]

OPTIONAL MARKETING CLAIMS [Appearing on any panel]

- For use on cats and kittens 8 weeks of age and older
- Advantage II contains [imidacloprid], [and an/the] [insect growth regulator] [IGR] [pyriproxyfen]
- A single topical application remains effective for up to [4 weeks] [a month]
- Convenient, easy-to-apply topical solution
- Convenient, easy-to-apply and fragrance free [monthly] [topical solution]
- Once a month topical flea prevention and treatment for cats 8 weeks of age or older
- Advantage II is indicated for the prevention and treatment of fleas on cats 8 weeks of age and older
- For the prevention and treatment of flea infestations
- One treatment prevents further flea infestations for up to [4 weeks] [a month]
- Kills fleas on cats within [12] hours and continues to prevent infestations for up to [four weeks] [a month]
- Kills fleas before they lay eggs
- Larval flea stages in the cat's environment are killed following contact with an Advantage II treated cat
- Kills larval stages of fleas following contact with an Advantage II treated cat
- Kills fleas within [12] hours of application
- Stops existing flea infestations by killing adult fleas
- Prevents reinfestations by killing adult fleas before they lay eggs
- Reinfesting fleas are killed within 2 hours with protection against further flea infestation
- [Prevents] [Stops] flea eggs from hatching [into biting adults]
- Effectively breaks the flea life cycle
- [Kills] [Controls] all flea life stages
- Comprehensive flea prevention and treatment
- 3-way flea protection ([kills] [controls]) adults, larvae, and eggs
- [Prevents] [Stops] flea eggs from developing into [(biting) (adult)] fleas
- Treatment with Advantage II kills fleas and may reduce the incidence of flea allergic dermatitis [FAD] or flea bite hypersensitivity
- Flea adulticide, larvicide, and ovicide
- Kills flea eggs
- Controls flea problems
- Provides flea protection
- Controls existing fleas and flea eggs plus [and] [prevents] future flea infestations
- Advantage II may be used year-round for flea [prevention][protection]

- Contains an insect growth regulator (IGR) to kill flea eggs and prevent re-infestation
- Monthly use of Advantage II kills fleas and may prevent ([flea allergy dermatitis][flea bite hypersensitivity])
- Controls existing flea infestations on your cat and prevents further infestations
- Prevents fleas on treated cats from infesting (reinfesting)
- Remains effective after bathing
- Remains effective following shampooing
- Waterproof
- Remains effective after exposure to rain or sunlight
- Fragrance-free
- In child-resistant packaging
- Starts working through contact

Pages 197-198 Confidential Statement of Formula may be entitled to confidential treatment